A PROSPECTIVE STUDY OF MAGNESIUM AND CALCIUM LEVELS IN SERUM AND CEREBROSPINAL FLUID IN COMMON NEUROLOGICAL DISORDERS

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C E R T I F I C A T E

This is to certify that the work entitled "A PROSPECTIVE STUDY OF MAGNESIUM AND CALCIUM LEVELS IN SERUM AND CEREBROSPINAL FLUID IN COMMON NEUROLOGICAL DISORDERS" has been carried out by Ajit Kumar Manocha, under my direct supervision and guidance in the Department of Paediatrics, M.L.B. Medical College, Jhansi.

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C E R T I F I C A T E

Certified that the work conducted by Ajit Kumar Manocha, entitled "A PROSPECTIVE STUDY OF MAGNESIUM AND CALCIUM LEVELS IN SERUM AND CEREBROSPINAL FLUID IN COMMON NEUROLOGICAL DISORDERS" was carried out under my supervision and guidance, by the candidate himself.

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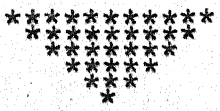
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INTRODUCTION

INTRODUCTION

Present century has ushered in an era of great biochemical advances. Strange though it may seem, practically every disease has now been shown to have some biochemical basis as the cause or its effect. Furthermore, besides other systems, the nervous system is greatly influenced by alterations in the concentration of major cations in the extracellular fluids. In this context role of sodium, potassium and calcium in the causation of various neurological manifestation is worth mentioning. Though considerable data exists regarding the derangement of calcium and magnesium metabolism in various other disorders, same is not true with respect to acute neurological diseases such as meningitis, encephalitis, epilepsy etc. Also, not much is known about the movement of these ions across the blood brain barrier.

Recent reports suggest, that there are alterations in serum and cerebrospinal fluid (CSF) levels of calcium and magnesium in tuberculous and pyogenic meningitis, encephalitis and epilepsy. Levels of magnesium are observed to be lower, while

calcium shows an increase. However, the prognostic value of these observations on the course and severity of meningitis has been ascertained by only a few authors. In view of this, it was our endeavour to evaluate the serum and CSF magnesium and calcium levels in meningitis, encephalitis and epilepsy in order to deduce a possible correlation, if any, between the concentration of these electrolytes and severity of various neurological disorders.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

HISTORY

Tuberculosis and tuberculous meningitis :

The ancient writings of Indian medicine reveal that tuberculosis has been existing in India for more than 2,000 years. Park and Park (1976) have mentioned that a detailed description of tuberculosis has been found in epics written by past masters like Hippocrates, Charak and Susruta but the cause of this disease has been steeped in ignorance and superstition. The authors have also referred the disease as "captain of the men of death" and "the great white plague". Authors further quote Hippocrates (400 B.C.), the father of medicine as calling it "Phthis" which means "to dry up". Robert Koch (1882) discovered the tubercle bacillus which ranks one of the most important discoveries in bacteriology and in the history of medicine. Ghai (1977) and Satya Gupta (1978) have commented that tuberculous meningitis is the most dreaded complication of tuberculosis and is the most common cause of death in infants and children suffering from tuberculosis.

Acute bacterial meningitis :

Acute bacterial meningitis, commonly known as pyogenic meningitis, was first described by Vieusseux (1805) while meningococcus, one of its important causative organism was first identified by Weichselbaum (1887).

Neal (1924) studied the incidence of acute bacterial meningitis in the age group of 10 years and older and found that the Neisseria meningitidis was the most common organism affecting about 76.7 percent of cases, followed by Diplococcus pneumoniae, Streptococcus, Staphylococcus and Haemophilus influenzae in that order of frequency. Scherling and Platou (1949) also found a similar incidence, with 65.7 percent of cases being caused by Neisseria meningitidis. Carson and Koch (1956) studied the incidence of acute bacterial meningitis in infants and children and found that Haemophilus influenzae was the most common infecting organism, followed by Neisseria meningitidis, Diplococcus pneumoniae, Escherichia coli, Salmonella, Staphylococcus, Streptococcus and others. Ziai and Haggerty (1958) reported that Escherichia coli was the most common causative organism of acute bacterial meningitis in neonatal group to be followed by Streptococcus, Staphylococcus, Diplococcus pneumoniae and others in order of frequency.

Encephalitis :

Japanese encephalitis has occurred in small epidemics in almost every region of Japan since 1891. Kaneko and Aoki (1928) designated this type of encephalitis as type B, to distinguish it from type A, the epidemic encephalitis of von Economo. Muckenfuss et al (1933) transmitted the disease to monkeys and mice, while Hayashi (1934) was the first to isolate the virus causing Japanese encephalitis type B. Inada (1937) also transmitted the virus to mice and monkeys and proved that it was filtrable. These workers also showed that it was immunologically distinct from the virus of the St. Louis epidemic.

Murray Valley encephalitis or Australian-x encephalitis occurred as an acute form of encephalitis in the late summer of 1917 and again in 1918 in Australia. Cleland, during the epidemics of 1917 and 1918, succeeded in isolating a virus from fatal cases and was able to produce encephalitis in monkeys by intracerebral innoculations.

A neurotropic virus has been isolated from blood and brain in a couple of human cases and from the mosquito (culex vishnuii) in the rural area of Tamil Nadu (I.C.M.R., 1975). This virus has been named as Tamil Nadu virus (T.N.V.) and has been closely allied to the virus isolated in the epidemics of encephalitis in Japan and Murray valley.

Equine encephalitis is not a new disease and has been observed in the United States for over 90 years. Meyer and associates (1931) first reported the discovery of a virus as the cause of encephalomyelitis among horses and mules in the San Joaquin valley of California. Later, Meyer (1932) was the first to suggest that man might become infected with the equine virus.

A tick-borne virus encephalitis known as Kyasanur forest disease of Mysore, was first recognized in 1957 in Karnataka state in South India (I.C.M.R., 1964). The causative virus has been shown to be identical with Russian spring encephalitis virus.

Epilepsy :

Another important neurological disorder commonly encountered in Paediatrics age group is epilepsy. Gibbs et al (1937) were the first to denote the term epilepsy and described it as "Paroxysmal cerebral dysrhythmia". Symonds (1959) tried to find out the various biochemical alterations leading to epilepsy and suggested that gama-aminobutyric acid may be a "natural anti-convulsant" formed in the brain which protects the individual from having convulsions. Posner et al (1969) and Beresford et al (1969) in another study to observe the effect of convulsions on brain metabolism, reported that cerebral metabolism increased during convulsions which lead to an increased need for oxygen and glucose by the brain.

DEFINITIONS :

Meningitis and encephalitis :

Meningitis is the term used to denote infection predominantly affecting the pia-arachnoid mater, while infection spreading to the brain substance is called encephalitis. Often both the structures are involved together when the condition is termed meningo-encephalitis. Infection usually spreads to the nervous system either directly from the neighbouring structures or via the blood stream. Steigman (1979) has opined that the term encephalitis often conjures up a picture of severe acute viral infection of the brain. In the actual clinical practice, however, this is too simplistic. Infectious and non-infectious causes, inflammatory and non-inflammatory reactions, and signs and symptoms arising from or having a secondary impact upon any portion of the central nervous system are often loosely considered 'encephalitic' from a general clinical stand point.

Epilepsy :

The term epilepsy and recurrent convulsive disorder can be used interchangeably. These terms designate a variable symptom complex characterized by recurrent, paroxysmal attacks of unconsciousness or impaired consciousness, usually with a succession of tonic or clonic muscular spasms or abnormal behaviour.

If a cause of the patients seizure cannot be found, he or she may be said to have idiopathic or cryptogenic epilepsy. However, if any cerebral abnormality is demonstrable, it is designated as organic or symptomatic epilepsy. Williams (1950), put forward the hypothesis that "a grand mal seizure seems to depend on a thalamic discharge which involves the non-specific reticular structures and is projected to the cortex in what may be considered as generalized recruiting response transmitted along the diffuse cortical projection pathways".

MAGNITUDE OF PROBLEM :

Meningitis, both tuberculous and pyogenic, and encephalitis still remain rampant in developing countries like India and form a considerable portion of total hospital admissions.

Tuberculous meningitis :

Extent of disease - The first national sample survey carried out by Indian Council of Medical Research (1959) showed the prevalence of tuberculosis to be about 7 per 1,000 in children 5 to 14 years of age. Of these, 0.3 per 1,000 were infectious. Subsequent surveys conducted by Pamara (1973) in Delhi and another one at the National Tuberculosis Institute, Bangalore in the year 1974, have shown a significant and continuous decline in the disease in children during the last 10 years or so.

Pattern of disease - Apart from the extent of disease, probably its pattern also varies from place to place. Bentley et al (1954) in a study conducted in U.K. reported that, out of nearly 1,000 tuberculous children admitted in the hospital, 47 percent had primary respiratory disease, 14.5 percent quiescent primary pulmonary lesions, 22 percent primary pleurisy, 2.5 percent miliary, 11 percent chronic pulmonary tuberculosis and 3 percent had miscellaneous lesions. Manchanda and Singh (1960) from a study in Amritsar reported the incidence of tuberculous meningitis to be 1.47%. Bharucha et al (1967) in a 4 year old study conducted at the K.E.M. Hospital, Bombay, from 1961-64, reported the incidence of tuberculous meningitis to be 4 percent of all the paediatrics admissions of a large teaching hospital. Bhakoo and Gupta (1969) reported the incidence of CNS tuberculosis as 1.8% from a study conducted at Chandigarh. In another study, conducted at New Delhi Tuberculosis Centre in the year 1974, nearly 50 percent of the freshly diagnosed tuberculous children had primary respiratory disease, 18 percent tuberculous lymphadenitis, pleurisy with effusion, 1.2 percent tuberculous meningitis, 12 percent chronic pulmonary tuberculosis and the remaining had the miscellaneous forms of the disease. Dingley (1976) in a study conducted at Mehrauli Tuberculosis Hospital, reported that primary disease was present in only 30 percent of the children admitted in the hospital and

chronic pulmonary disease was seen in 60 percent of the children. The remaining 10 percent had mainly miliary and meningeal types of the disease.

Acute bacterial meningitis :

Large scale reports and statistics, from India and other developing countries, concerning acute bacterial meningitis are rather meagre. Achar (1982), observed the incidence of acute bacterial meningitis admitted to paediatrics ward in Thanjavur medical college and Rajamirasdar hospital during 1966-73, to be 1.6 percent with a mortality rate of 34 percent. In this study, 47.1 percent were below 1 year of age while 18.4 percent, 16.5 percent, 12.5 percent and 5.3 percent were found in 1-3 year, 3-5, 5-10 and above 10 year age groups respectively. Further, he quoted that, in Erskine Hospital, Madurai, the incidence of acute bacterial meningitis was found to be 1.9 percent with a mortality rate of 38.3 percent during the period 1970-73.

Encephalitis :

Kyasanur forest disease (KFD), a tick borne virus encephalitis, was first recognized in Karnataka state in South India (I.C.M.R., 1964). A serological survey conducted by I.C.M.R. (1964) on man and domestic animals in other parts of India, indicate that KFD and other related viruses might be widespread in the country.

Arora (1974) reported an epidemic of Japanese encephalitis in West Bengal resulting in about 839 cases with a case fatality rate of over 50 percent. Serological surveys carried out by the Virus Research Centre, Poona (I.C.M.R., 1975) indicated that Japanese encephalitis virus (also called Tamil Nadu Virus - TNV) was one of the most widely prevalent arboviruses in India. In this study it was found that about half of the population in South India had neutralizing antibodies to this virus. Park and Park (1976) have said that Japanese encephalitis is a public health problem along the east coast of India - Krishna Godavri delta, Bengal, the foot hills of the NEFA and the Brahmputra valley in Assam.

Epilepsy - Females have been said to suffer from epilepsy slightly more frequently than males. However, Lennox and Lennox (1960) found, that while under the age of 5 years, there were 105 females for every 100 affected males, over the age of 20 years the ratio of male and female incidence was 100 : 59. Pond et al (1960) and Brewis et al (1966) have reported that in the United Kingdom the number of epileptics was estimated to be about 3 lakhs, with about 35 thousand new cases occurring annually. In India a collective data regarding the incidence of epilepsy is not available. Brain (1977) has opined that the commonest age of onset is 0-4 years, with the first fit occurring in many more patients between

5 and 24 years of age, the incidence of initial attack then declines steadily throughout adult life.

PHYSICAL CHARACTERISTICS (CLINICAL FEATURES)

Tuberculous meningitis :

Tuberculous meningitis is usually insidious in onset but may be fulminant if a caseous lesion discharges directly into the subarachnoid space. Heinz and Thomas (1979) grouped the clinical manifestations of tuberculous meningitis into 3 stages -

Stage 1 (general, non-specific symptomatology),

Stage 2 (appearance of definite neurologic signs) and

Stage 3 (coma).

Stage 1 : This is characterized by irritability, disinterest in play, idly staring in space, fever, headache, vomiting, anorexia and constipation.

Stage 2 : This is characterized by convulsions, signs of meningeal irritation, cranial nerve palsies and features of raised intracranial tension in form of buldging anterior fontanelle or crack pot sound over head. Fundus examination may reveal papilloedema and optic disc may show primary or secondary atrophy.

Stage 3 : In this stage there is unresponsiveness, opisthotonus, decerebrate rigidity and paralysis.

The most common neurologic sequelae are developmental retardation, cranial nerve palsies, hydrocephalus, optic atrophy, deafness, paralysis, continuing stupor or coma, convulsions and pituitary disturbances.

Acute Bacterial Meningitis :-

Smith (1956) studied the clinical features of acute bacterial meningitis in infants and children. He found that it was much more difficult to recognize acute bacterial meningitis in young infants because of the paucity of typical meningeal signs. The author found that most of young infants manifested with cyanosis, fever, vomiting, jaundice, irregular breathing and irritability or drowsiness, while older infants manifested with fever, vomiting, irritability or drowsiness, convulsions and buldging anterior fontanelle. The author further reported that the children above 2 years of age presented with typical symptoms and signs of meningeal irritation such as fever, headache, vomiting, drowsiness, neck stiffness and convulsions.

Tobin (1956) studied the complications and sequelae of acute bacterial meningitis. He classified the complications into two broad groups (1) those secondary to bacteremia; (2) those relating to the involvement of the nervous system. The first group

included lesions produced by the lodging of organisms in various portions of the body outside the central nervous system, and consisted of pneumonia, endocarditis, pericarditis, nephritis, arthritis and iridocyclitis. Complications included in the second group were the result of inflammatory changes in the central nervous system. These included cranial nerves involvement including deafness and blindness, hemi or quadriparesis, muscular hypertonia, ataxia, permanent seizure disorders, subdural effusions and the development of obstructive hydrocephalus, mental retardation or learning disabilities. Rabe et al (1968) & Menkes (1974) reported that persistent pyrexia, and increased intracranial pressure 72 hours after the start of treatment in infants should make one suspect the presence of a subdural effusion.

Encephalitis :

After a short incubation period of five to ten days, the disease is characterized by sudden onset of high fever, headache, nausea and vomiting. Convulsions are important signs of CNS irritability especially in infancy. Stupor, lethargy and coma are signs of CNS depression. At times, bizarre behavioural disturbances or hyperactivity may be the signs of CNS involvement. Cranial nerve paralysis and hemiplegia are occasionally seen.

Infants who recover may develop sequelae like mental retardation, convulsions and hydrocephalus.

Grand mal epilepsy :

Grand mal epilepsy is often preceded by an aura and the attack may be precipitated by a number of factors, including fever, fatigue, hyperventilation, flashing lights, and even by a sudden gush of hot water when bathing, as described by Mani et al (1973). Further as the author reports it is characterized by loss of consciousness, a tonic phase, followed by a clonic phase and finally ending in stupor, confusion or ataxia.

DIAGNOSIS :

Tuberculous Meningitis - The diagnosis of tuberculous meningitis is based on certain supportive and diagnostic criteria. The supportive tests primarily include a positive tuberculin skin test and an X-ray chest showing a primary focus. Lincoln (1947) and Lincoln and Sewell (1963) studied the incidence of positive montoux test in cases of tuberculous meningitis. In both the studies, authors found that montoux test was positive in about 85 percent of cases of tuberculous meningitis. The diagnostic criteria includes a CSF examination, which invariably shows an abnormal spinal fluid. Heinz and Thomas (1979) have opined that white blood cells in CSF are usually fewer than 350/cubic mm. and consists

primarily of mono-nuclear cells, but in few cases the fluid showed upto 1000 cells, with a predominance of polymorphonuclear leucocytes. Wright (1953) showed that by the time the disease was well established the sugar was usually below 45 mg/100 ml. and though in the early stages protein concentration was normal or slightly elevated, but with time it increased to 300 mg/100 ml or more. Gierson and Marx (1955) studied the significance of chloride estimation in the diagnosis of tuberculous meningitis. These authors reported that the chloride content almost always fell below 115 mEq and occasionally as low as 110 mEq per litre, the values tend to become lower as the disease progressed. Now this test is not regarded to be specific for tuberculous meningitis. Heinz and Thomas (1979) said that the change in CSF chloride reflects levels of serum chloride which are depressed because of inappropriate antidiuretic hormone secretion or more rarely, because of protracted vomiting. If an aliquot of spinal fluid is allowed to stand undisturbed for several hours, a pellicle may form. Organisms are most readily seen within the matrix of the pellicle and can also be readily cultured from this material. Thapar (1967) observed that isolation of tubercle bacilli from the CSF varies with different techniques - 3% by ordinary centrifuge method, 38.8% by precipitation of deposit from CSF by alcohol and 79% by floatation hydrocarbon technique.

Septic Meningitis :

Changes in cerebrospinal fluid occur early in acute bacterial meningitis. Levinson (1925) made a comparative study of sugar content of blood and of cerebrospinal fluid in various conditions. He found marked depression of CSF glucose and of the CSF : blood glucose ratio (normally about 66 percent) in cases of septic meningitis. Fremont and Dailey (1932) also reported the low level of CSF glucose in acute bacterial meningitis. Merritt and Fremont (1938) studied the changes in CSF protein, sugar, chlorides and cell count in meningitis. The authors reported a white cell count of 1,000 to 10,000 per cubic millimeter with the predominance of polymorphonuclear leukocytes and a rise in protein content in cerebrospinal fluid. Baltch and Osborne (1957) studied the causes of lowered sugar level in CSF in acute bacterial meningitis. They found out that the lowered sugar content was mainly due to the glycolytic action of the bacteria and the presence of leukocytes alone did not significantly alter the sugar level.

Quellung and agglutination reactions can provide immediate identification of various organisms if they are visible on smear and if appropriate type-specific antisera are available. Hurley and Wagner (1972) studied the diagnostic value of brain scanning in children. They were of the view that radio-isotope scanning might be helpful

in few patients and the pattern of distribution of radioactivity recorded by gamma camera coincided with the accumulation of purulent material. Shackelford et al (1974) evaluated the role of countercurrent immuno-electrophoresis (C.I.E.) in the diagnosis of childhood infections. The authors found that CIE had proven to be a useful technique for the rapid (within 1 hour) diagnosis of bacterial meningitis due to H.influenzae type b, S.pneumoniae, and N.meningitidis groupa A, C and D. This technique could also detect the nonviable bacteria. A negative counter current immuno-electrophoresis result would not exclude the diagnosis of bacterial meningitis.

For the identification of bacteria Heinz and Thomas (1979) suggest cerebrospinal fluid culture on a blood agar plate, a chocolate agar plate on Fildes or Leventhal medium, and in broth. Further, authors have opined that when meningitis is suspected, the CSF should be cultured even if it is crystal clear and acellular, since bacteria could be present before pleocytosis or chemical changes became apparent. Heinz and Thomas (1979) have further opined that the limulus lysate assay is a valuable adjunct to diagnosis permitting the diagnosis of endotoxin within the cerebrospinal fluid. A positive test indicates meningitis with gram-negative organisms. Further it has been suggested that blood cultures should be obtained in every case. When the concentration of bacteria within the blood is high, a gram stained smear could reveal

the presence of micro-organisms. If petechial rashes are present, a smear of the lesions following puncture with a small lancet could reveal micro-organisms on gram's stain. Bachman et al (1977) studied the value of computerized axial tomography (CAT) in the diagnosis of neurological disorders in the children. This non-invasive technique permits detection of ventricular dilatation, subdural effusion, decrease in brain mass, and the presence of vascular lesions or of brain infarcts.

Viral Encephalitis :

Brain (1977) is of the opinion that in viral encephalitis the CSF was generally clear; the leucocyte count ranged from none to several thousand, often with a significant percentage of polymorphonuclear cells initially, moderate or no elevation of protein, and an initially normal level of glucose in ratio to the simultaneously determined blood glucose levels. In any patient suspected of having viral meningo-encephalitis spinal fluid, blood, faeces and throat swabs should be collected and sent to laboratory offering viral diagnostic services. An additional serum specimen should be collected 10-14 days later. Though these studies gave no immediate diagnostic assistance, they were useful because etiologic diagnosis might give early warning of a specific epidemic. Dayan and Stockes (1973), Lindeman et al (1974) and Legg (1975) studied the value of immuno-fluorescent techniques for the

early diagnosis of encephalitis. These authors found that immuno-fluorescent techniques for the identification of specific antibodies could be applied to brain biopsy sections or to cells isolated from the cerebro-spinal fluid.

Epilepsy :

Brain (1977) opined that in idiopathic epilepsy the CSF was normal except that during or after frequent fits or an attack of status epilepticus, there might be a rise in pressure to above 200 mm. of fluid and a modest rise in protein content of the fluid. The author further said that a consistently raised CSF protein and a pleocytosis suggested that the epilepsy was symptomatic. The author further opined that electro-encephalography (EEG) might be helpful in the diagnosis of epilepsy and an abnormal record obtained in the interval between the attacks established the diagnosis when this was otherwise in doubt. Gibbs et al (1937) reported that an abnormal EEG could be interpreted only in relation to clinical history of the patient as the non-specific abnormalities might be found in epilepsy, psychoneurosis, psychopathy or psychosis. This observation was later supported by Williams (1941). Air encephalography and/or ventriculography usually gave normal findings in cases of epilepsy, but Hunter et al (1962) reported signs of ventricular dilatation and cortical atrophy in some cases of long standing epilepsy and epilepsy of late onset.

Gamma encephalography and computerized transaxial tomography (CTT scan) are likely to play an increasing role in the investigation of epileptic patients in order to exclude the presence of cerebral lesion, of which the epilepsy may be symptomatic. Wallace (1974) who studied 132 patients with late-onset epilepsy, using gamma encephalography found that 26 had abnormal scans, due to tumor, abscess, infarction or trauma.

RECENT DIAGNOSTIC TESTS :

CSF lactic acid estimation :

Levinson (1917) was the first to report the decreased pH of CSF in pyogenic meningitis. Later, Nishimura (1924) reported the increased levels of lactic acid in CSF in cases of pyogenic meningitis. This finding was also confirmed by Killian (1925), De Sanctis et al (1933), Controni et al (1971), Bland et al (1974), Gandhi et al (1977) and Singhal et al (1981). Singhal et al (1981) reported that the level of lactic acid was significantly higher in pyogenic meningitis (71.64 $\pm$ 39.20 mg%) as compared to values observed in tuberculous meningitis (36.42 $\pm$ 2.92 mg%), encephalitis (19.50 $\pm$ 5.50 mg%) and controls (10.65 $\pm$ 3.52 mg%). In cases of tuberculous meningitis, the level was significantly higher than in cases of encephalitis and controls. Thus, the authors found a considerable overlap in lactic acid levels in various types of meningitis, limiting its diagnostic value.

The authors attributed the excess of lactic acid to anaerobic glycolysis and tissue anoxia.

Bromide test - Walter (1929) was the first to use unlabelled bromide in the diagnosis of tuberculous meningitis by determining the plasma/CSF ratio. This procedure was, however, very tedious, hence Crooks et al (1960) advocated the use of labelled bromide to simplify the technique. Bharucha et al (1980), also reported the usefulness of this procedure in the diagnosis of tuberculous meningitis. 0.6 microcurie/kg body weight of 82-bromide dissolved in water was given by mouth and 48 hours later, an equal volume of plasma and CSF were counted in a sodium iodide well counter to determine the plasma/CSF ratio. The authors observed that a ratio of 1.6 or lower was diagnostic of tuberculous meningitis.

CSF glutamic oxalo-transaminases estimation :

Green et al (1957) reported the increased levels of enzyme glutamic oxalo-transaminases (G.O.T.) in CSF in cases of pyogenic meningitis. Later, this was also confirmed by Belsey et al (1964), Reddi et al (1976) and Praharaj et al (1979). Praharaj et al reported the mean normal CSF-GOT level to be 6.47 IU/L (range 2 to 11 IU/L) and the levels of CSF-GOT were significantly raised in pyogenic meningitis than in tuberculous meningitis. However, the authors observed that the CSF-GOT level was slightly more in cases of tuberculous meningitis than the

controls. On serial estimations of CSF-GOT levels, the authors found that the levels gradually came to approximate normal levels as the patient improved. The authors did not find any relationship between the initial CSF-GOT levels and the prognosis of the case. The authors attributed the high levels of enzyme in CSF to changes in CSF/blood barriers, to the damage of brain tissue, to the presence of leucocytes or bacteria in CSF or to a combination of all the above factors.

CSF lactic dehydrogenase (LDH) estimation :

Jakoby (1959) reported the elevated levels of LDH in CSF in acute bacterial meningitis and observed that it returns to normal after treatment. Later, this was confirmed by Lending et al (1964), Williams and Hawkins (1968), Belsey (1969), Khanna et al (1977) and Gupta et al (1982). Gupta et al (1982) in an extensive study estimated the LDH activity in serum and CSF in 100 patients with different neurological disorders and 20 control cases between the ages of 1 month and 12 years. The authors found that the normal mean serum level was 151.70 $\pm$ 90.06 while normal mean CSF value was 25.96 (range of 3 - 47). The authors found a definite increase in LDH activity in cases of acute bacterial meningitis as compared to viral central nervous system infections. A consistently increased activity was also noted on serial estimations of LDH in CSF of patients who developed sequelae or expired as

compared to those who received or reported early in the disease process. However, the authors were of the view, that to attribute the prognosis to the high values of enzyme alone might not always be true and other factors had to be considered which could shape the final outcome of disease.

CSF-immunoglobulins :

O'Toole et al (1971) reported a rise of CSF IgG and IgA levels in CNS infections, the rise being more in bacterial than in viral infections. The authors also reported that the patients with pneumococcal meningitis had higher IgG levels than those with meningococcal meningitis. Smith et al (1973) also reported similar findings. Varavi et al (1982) estimated CSF immunoglobulins in cases of pyogenic meningitis, tuberculous meningitis and viral encephalitis. Cases of tetany, epilepsy and febrile convulsions served as controls in this study. The authors observed that the values of IgG, IgM and IgA were significantly higher in TBM, pyogenic meningitis and viral encephalitis than the controls, where very low values of IgG and absence of IgM and IgA were seen. On a further analysis, they reported that the values of CSF immunoglobulins were significantly higher in both pyogenic and tuberculous meningitis than in cases of viral encephalitis, though no statistically significant difference was observed between TBM and

pyogenic meningitis. Further, the authors found that the ratio of IgG/Protein in TBM was significantly higher than in cases of pyogenic meningitis and hence it would be useful in differentiating between the two disorders.

CSF-Sialic acid estimation :

Balasubramaniam et al (1974), Tausif et al (1976) and Din et al (1981) reported the increased levels of free sialic acid in cases of meningitis of pyogenic origin. Din et al (1981) found the free sialic acid levels in controls to be 0.31 $\pm$ 0.13 mg/100 ml, while it was 2.6 $\pm$ 0.26 mg/100 ml and 0.38 $\pm$ 0.03 mg/100 ml in cases of pyogenic meningitis and tuberculous meningitis respectively. The authors found that the levels of free sialic acid remained high even after partial treatment with antibiotics. The authors attributed the high levels of CSF free sialic acid in pyogenic meningitis to the action of bacterial neuraminidase on glycoproteins and gangliosides of nervous system.

CSF C-reactive protein :

James et al (1981) reported the role of C-reactive protein in the diagnosis of pyogenic meningitis. The authors used the latex agglutination test for detection of C-reactive protein in CSF. On initial lumbar puncture, they detected C-reactive protein in 100% of patients with bacterial meningitis as compared to 6% ($P < 0.001$) of patients in non-bacterial group. Thus, the authors

concluded that C-reactive protein in CSF had a sensitivity of 1.0 and a specificity of 0.94 for detecting culture positive bacterial meningitis. The authors further said that CSF C-reactive protein estimation had proved to be more sensitive test for differentiating bacterial from non-bacterial meningitis on initial CSF examination than was the number of CSF leukocytes, the absolute number of CSF polymorphonuclear leukocytes, CSF glucose concentration, CSF protein concentration or gram staining of CSF.

STUDY OF MAGNESIUM AND CALCIUM LEVELS IN NEUROLOGICAL DISORDERS :

Meningitis and Encephalitis :

Cohen (1923) was the first author to draw attention to the changes in concentration of various substances in plasma and CSF in meningitis, as well as the various factors governing their permeability across the blood-CSF barrier. He was of the view that changes in concentration of the various substances vis-a-vis plasma, in meningitis was partly dependent on its quantity in the two compartments. In this study he made the following observations :-

1. There was an increasing concentration in CSF of those substances which were normally present in greater quantity in blood-plasma than in the CSF e.g. proteins phosphates, cholesterol, calcium and uric acid.

2. There was an appearance in CSF -

 a) of substances which were normally present in blood but absent from CSF e.g. fibrinogen, bile pigment and complement.

 b) of foreign substances injected into the blood stream which normally did not pass into the CSF e.g. iodides, methylene blue, fluorescein, meningococcus antibodies and salicylates.

3. There was a decreasing concentration in CSF of those substances which were normally present in greater quantity in CSF than in the plasma, to this group belonged the chloride ion.

Later Cohen (1927), in an extension of the previous study evaluated the concurrent changes in concentration of calcium and magnesium in serum and CSF in cases suffering from tuberculous meningitis. He carried out the work on 18 children and observed that the CSF magnesium in normal and pathological states other than meningitis, had mean values of 3.28 mg/100 ml, which were constantly greater than the contemporary blood serum values of 2.56 mg/100 ml. He further observed that in cases of meningitis, on the other hand, the excess of magnesium in CSF was less marked. He attributed these changes to increase in the permeability of choroid plexus and cerebrospinal vessels which were damaged by invading

organisms or toxins. Cohen further observed that the magnesium content of CSF was independent of the age or sex of the patient, cell or protein content of the fluid and wassermann reaction of the fluid.

Mc Cance and Watchron (1931) subsequently reported, that the concentration of magnesium in CSF was very constant and usually higher than that found in the serum. They observed that the levels of magnesium in CSF in 60 normal children had mean value of 3.33 mg/100 ml with an average deviation of $\pm$ 0.19. He further reported that the percentage of magnesium in cerebrospinal fluid was not altered by the presence of excess of protein, by syphilis or by wide variations in serum levels. On further analysis of the magnesium and calcium concentrations in CSF of children suffering from tuberculous meningitis, the authors reported that while the magnesium concentration was low in these cases, no change or shift was observed in the calcium levels in the CSF.

Kabat et al (1942) tried to correlate the changes in CSF electrolytes to the chemical changes in the CSF. He reported that the concentration of calcium in the CSF was directly correlated to the elevation of proteins, an increase of proteins in the CSF was associated with a concomitant rise of calcium in the CSF. Chojnacki (1956) also studied the serum and CSF magnesium levels in normal controls and in cases of tuberculous meningitis.

He also found higher magnesium levels in CSF than in serum in normal controls. The author suggested that the higher concentration of magnesium in CSF in comparison to that of serum might be due to the contribution of the magnesium rich central nervous system, to the CSF through the perivascular and perineuronal spaces. The author further found that the CSF magnesium level was reduced in cases of tuberculous meningitis.

Wright (1956) studied the physiology of regulation of CSF ions. He stated that the cells of choroid plexus actively regulated the transfer of ions and other crystalloids.

Chhaparwal and Pohowalla (1966) studied the magnesium levels in serum and cerebrospinal fluid in children and also reported significantly low values of CSF magnesium in cases of tuberculous meningitis, epilepsy and meningo-encephalitis in comparison to controls.

Rajvanshi et al (1970) carried out an extensive study of the serum magnesium levels in some common paediatrics problems, which included nephrotic syndrome, infantile liver cirrhosis, tuberculous meningitis and encephalitis. The authors observed that the serum magnesium values in 8 cases of tuberculous meningitis and 10 cases of encephalitis ranged from 1.2 to 2.3 and 1.2 to 2.2 mEq/l respectively, with a mean of 1.8 and 1.7 mEq/l

respectively. It was seen from this study that 3 cases of tuberculous meningitis out of the 8 studied and 3 cases of encephalitis out of the 10 studied had hypomagnesemia. The authors said that perhaps the severity of tuberculous meningitis and encephalitis had some correlation to the decreased concentration of magnesium in serum, since lowest values of serum magnesium (1.2 mEq/l) was seen in a child who had the third relapse of meningitis, while in encephalitis the two cases who demonstrated the lowest values were both having severe degree of vomiting and diarrhoea. The authors, however, failed to derive any correlation between the hypomagnesemia and the neurological manifestations.

In another extensive study, Misra et al (1973) estimated the contemporary magnesium and calcium levels in blood and CSF. Twenty two children suffering from tuberculous meningitis and seventeen patients having pyogenic meningitis were included in this study. Authors observed, that in normal children which served as controls in their study, values of CSF magnesium were higher than that in serum, while the reverse was true for calcium. The values were as follows :-

	Serum magnesium	CSF magnesium	Serum calcium	CSF calcium
Controls	1.83 mEq/l (± 0.17)	2.45 mEq/l (± 0.33)	4.93 mEq/l (± 0.29)	2.38 mEq/l (± 0.22)
Tuberculous meningitis	1.63 mEq/l (± 0.30)	2.05 mEq/l (± 0.15)	4.88 mEq/l (± 0.10)	2.47 mEq/l (± 0.15)
Pyogenic meningitis	1.60 mEq/l (± 0.35)	1.86 mEq/l (± 0.14)	4.92 mEq/l (± 0.30)	2.61 mEq/l (± 0.25)

The authors reported that in tuberculous meningitis magnesium values were significantly lower than that in healthy children both in serum and CSF (P value < 0.001), but the calcium levels showed a statistically insignificant increase in the CSF. Unlike the previous study, the authors, however, did not observe any apparent correlation of the magnesium level to the severity of disease either on the clinical grading or to the chemical constituents of CSF. Authors, however, found a longer duration of illness conducive to the development of hypomagnesemia.

Regarding septic meningitis Misra et al (1973) observed that there was a decrease in CSF magnesium and an increase in CSF calcium in comparison with the normal controls. Further the authors observed the lowest CSF magnesium values in those patients with septic meningitis who had a thick purulent CSF during the course of illness. Thus the authors concluded, that it was only in the presence of a marked rise of CSF proteins that the magnesium levels showed a significant lowering, while a mild to moderate rise in CSF proteins failed to show any correlation with magnesium drop. Finally, the authors related these changes in cases of septic and tuberculous meningitis to the altered state of blood brain barrier, whereby the CSF tends to approximate to blood plasma in chemical composition.

Ahmad et al (1977) estimated serum and CSF magnesium and calcium levels in 23 patients of tuberculous meningitis and 15 normal controls. The mean serum and CSF magnesium levels in control subjects were 1.995 mEq/l and 2.396 mEq/l. The respective values in patients of tuberculous meningitis were 1.265 $\pm$ 0.453 mEq/l and 1.373 $\pm$ 0.472 mEq/l. On statistical analysis both serum and CSF magnesium levels were found to be significantly low ($P < 0.001$) in cases of tuberculous meningitis. Authors observed an inverse correlation of CSF magnesium with CSF proteins and cells, while CSF sugar was found to run parallel to the magnesium level. Contrary to earlier findings (Misra et al, 1975), the present authors found that low magnesium level in tuberculous meningitis carried a poor prognosis especially when associated with an advanced state of illness. Authors also concluded that low CSF magnesium content in tuberculous meningitis cases was related to hypomagnesemic states. Authors did not observe any significant alteration in serum and CSF calcium levels of the patients and normal controls.

Kumar et al (1981) made concurrent serial estimations of sodium, potassium, calcium and magnesium in plasma and CSF of 27 cases of tuberculous meningitis and of 21 normal children serving as controls. The authors observed that in controls, plasma and CSF calcium

levels were 4.69 ± 0.69 and 3.00 ± 0.33 respectively, the corresponding values observed in cases of tuberculous meningitis were 5.57 ± 0.82 and 3.93 ± 0.54 ($P < 0.001$ and 0.001 for plasma and CSF respectively). Authors further observed that plasma and CSF calcium values decreased with treatment, but still plasma calcium levels remained higher after three weeks of treatment ($P < 0.001$) than corresponding controls. Authors supported the earlier reports (Kabat et al, 1942) which concluded that CSF calcium was elevated along with increased proteins in the CSF. Kumar et al (1981) further observed that in controls, plasma and CSF magnesium levels were 2.21 ± 0.23 and 2.39 ± 0.25 respectively, the corresponding values observed in cases of tuberculous meningitis were 2.00 ± 0.30 and 1.68 ± 0.80 ($P < 0.001$). On subsequent estimation authors observed a rise in CSF magnesium while plasma magnesium did not reveal any change. Authors concluded that with the treatment, CSF magnesium level increased presumably because of contribution of magnesium from an auxillary source through brain-CSF-blood barrier. Regarding low CSF magnesium levels in tuberculous meningitis authors attributed it to be due to the blocking of the contribution of extra magnesium from the brain into CSF pool and not to the hypomagnesemia as postulated by previous workers (Ahmad et al, 1977). The authors did not study the prognostic significance of these changes in tuberculous meningitis cases.

Praharaj et al (1982) also studied serum and CSF magnesium levels in pyogenic and tuberculous meningitis in children. 20 control cases, 32 cases of tuberculous meningitis and 20 cases of pyogenic meningitis were included in this study. In the control group, the mean serum and CSF magnesium was 1.92 mEq/l $\pm$ 0.02 and 2.80 mEq/l $\pm$ 0.20 respectively, values in the CSF being much higher and the difference being statistically significant ($P < 0.001$). The authors further stated that there was no significant difference in serum and CSF magnesium values among the different age groups and sexes ($P > 0.05$). The authors attributed the higher concentration of magnesium in CSF as compared to that of serum due to the contribution by the perivascular and perineural spaces or the cells of choroid plexus actively regulating the transfer of ions and crystalloids. The authors further observed that serum and CSF magnesium in tuberculous meningitis cases were 1.70 $\pm$ 0.28 and 2.31 $\pm$ 0.30 respectively, which were significantly low as compared to controls ($P < 0.001$) and there was a significant rise of magnesium levels in serum and CSF at the time of discharge after recovery ($P < 0.001$). Similarly, in pyogenic meningitis authors observed that serum and CSF magnesium values were 1.84 $\pm$ 0.31 and 2.18 $\pm$ 0.31 respectively which were significantly lower than the control group and values gradually increased with recovery. Thus, the authors found that CSF magnesium tended to approximate with blood

plasma levels in meningitis and regarded these changes as a consequence of an increased permeability of the cells of chroid plexus and cerebrospinal fluid vessels when those were damaged by invading organisms or toxins. The authors further tried to correlate the CSF magnesium values with the chloride and the protein content of CSF. The correlation between CSF magnesium and chloride levels revealed that CSF magnesium level fell in parallel with fall of chlorides. The mean CSF magnesium was 2.87 mEq/l when the chloride level was more than 700 mg% and it came down to 1.82 mEq/l with the chloride decreasing to 600 mg%. Thus, authors observed a strong correlation between magnesium and chloride levels statistically ($r = + 0.90$). Again the authors observed an inverse relationship between the protein and magnesium levels in CSF in pyogenic meningitis, but no definite correlation could be obtained in those cases where protein was less than 90 mg%. Finally, the authors observed that the serum and CSF values of magnesium gradually rose as the clinical and biochemical recovery proceeded and hence concluded that the magnesium estimation helped to know the progress of the disease as well as the response to treatment.

Epilepsy :

Hanna et al (1960) studied the serum and CSF magnesium levels in cases of idiopathic epilepsy and reported low levels of magnesium in both the body fluids in majority of cases as compared to controls.

Chhaparwal and Pohowalla (1966) reported that 6 out of 9 children with epilepsy had lowered CSF magnesium levels.

Similar findings had been reported by Jain et al (1968).

Wong et al (1968) studied 40 cases of convulsions, tremors or muscular twitchings and found low serum levels of magnesium in most of cases. The authors suggested that hypomagnesemia stimulated the parathyroid glands, elevating the blood calcium levels, a combination of hypomagnesemia and hypercalcemia might act synergistically in facilitating acetyl choline release, thus accounting for neuromuscular irritability.

Kumar et al (1979) studied serum and CSF sodium, potassium, calcium and magnesium levels in cases of febrile convulsions, grandmal seizures, focal seizures and minor motor seizures. 21 normal children served as controls in this study. The authors reported that concurrent serum and CSF sodium, potassium and calcium did not show any significant variation from that of controls. The authors reported the values of serum and CSF magnesium in controls as 2.20 mEq/l $\pm$ 0.23 and 2.43 mEq/l $\pm$ 0.26 respectively and the corresponding values in patients of epileptic disorders was 1.789 $\pm$ 0.15 and 1.887 $\pm$ 0.27 respectively. The authors further stated

that in epileptic disorders a significant reduction (P value $\leq$ 0.005) in CSF magnesium levels below 1.5 mEq/l was found in 20% cases. The authors concluded that the lowered CSF magnesium in idiopathic epilepsy might be the possible etiopathogenetic mechanism in the production of convulsions in children.

MATERIAL AND METHODS

MATERIAL AND METHODS

The present study was carried out in the Department of Paediatrics, M.L.B. Medical College, Jhansi, in collaboration with the Department of Biochemistry, M.L.B. Medical College, Jhansi, over a period of 11 months from May 1981 to March 1982. Children from birth to 12 years of age admitted in the Paediatric ward, were selected for this study. Cases were grouped as :

A : Controls - children not manifesting any neurological disorder.

B : Cases of tuberculous meningitis.

C : Cases of pyogenic meningitis.

D : Cases of encephalitis.

E : Cases of grand mal epilepsy.

Selection of controls -

Eight children from birth to 12 years, not manifesting any neurological disorders were taken as control for the present study. Children from birth to 12 years of age recovering from upper respiratory infections or bronchopneumonia or primary tuberculosis who had not suffered in the past with convulsions,

meningitis or encephalitis or liver diseases were taken as control subjects.

Selection of cases of tuberculous meningitis -

Fifteen cases of tuberculous meningitis were taken for the present study. The diagnosis of tuberculous meningitis was based on history, clinical findings and CSF examination. In most of the cases X-ray chest was done to find out the evidence of primary focus.

Selection of cases of septic meningitis -

Seven cases of septic meningitis were taken for the present study. Diagnosis of septic meningitis was also based on history, clinical and CSF examinations. Besides biochemical examination of CSF, smear for gram staining and CSF culture and sensitivity was also done in each case.

Selection of cases of encephalitis -

Nine cases of encephalitis were taken for the present study. Diagnosis of encephalitis was based on a short history of fever, generalised convulsions followed by unconsciousness. Clinically these children presented with varying degrees of neurological deficit and some had a fatal outcome. The diagnosis was substantiated by a normal CSF examination in all the cases.

Selection of cases of grand mal epilepsy -

Nine cases of grand mal epilepsy were taken for the present study. The diagnosis of grand mal epilepsy was based on history and clinical findings - i.e. children presenting with generalized convulsions, usually with tonic and clonic phases of the muscular spasms associated with loss of consciousness and usually recovering within 24 hours. In addition, CSF examination, X-ray chest, X-ray skull and montoux test were also done in a few cases to rule out secondary or organic epilepsy, whenever indicated.

Children suffering from tuberculous or pyogenic meningitis, or encephalitis or grand mal epilepsy were treated as follows :-

a) Tuberculous meningitis - The cases of tuberculous meningitis were treated with anti-tubercular treatment and steroid. Intravenous fluids, anticonvulsants and drugs to reduce raised intra-cranial tension such as glycerol and mannitol were used as and when required.

b) Septic meningitis - The cases of septic meningitis were treated with broad spectrum antibiotics and later specific antibiotics were started after culture and sensitivity. In addition, other supportive treatment was given as in tuberculous meningitis.

c) Encephalitis - The cases of encephalitis were treated by intravenous fluids, broad spectrum antibiotics and steroids. Other supportive measures were given as in cases of tuberculous meningitis.

d) Epilepsy - The cases of epilepsy were generally treated by giving anti-convulsants such as sodgardinal, diazepam or other anticonvulsants were given in addition or substitution as and when required. In addition other supportive measures were given as and when required.

An attempt was made to follow the cases of tuberculous or pyogenic meningitis or encephalitis at five to ten days interval thrice during and following recovery.

During each follow-up a detailed clinical examination and CSF examination was done. Other investigations were done as and when necessary. In each case besides name, age, sex, address, antenatal, natal and postnatal history, socio-economic status, developmental history and dietary history following facts were recorded.

Immunization status -

History of immunization was taken from the parents or family members. For smallpox and B.C.G. vaccination confirmation was made by careful inspection of scar marks. For polio and DPT vaccination, however,

verbal statements were relied upon and confirmed from records whenever available.

Present, past and family illnesses -

A detailed account of the history of present illness, past and family history was taken in each case. Special emphasis was given to obtain the history of onset of disease, history of fever, headache, vomiting, unconsciousness, convulsions and paresis or paralysis of any part of body. Efforts were also made to find out the various important past illnesses, such as definite history of primary tuberculosis, measles, pertusis, ear discharge, head injury or convulsions which could have precipitated or helped in diagnosis of present illness.

An enquiry was made about the history of any familial illness such as tuberculosis and convulsion.

Physical examination -

A thorough clinical examination was done in each case. General physical examination included, a general appearance of the patient, for evidence of pallor, anaemia, any significant lymphadenopathy and for any obvious septic focus in the body. Anthropometric measurements were recorded in each case and special emphasis was given to record the serial head circumference to evaluate the possibility of developing hydrocephalus.

Central nervous system was examined in full detail. Level of consciousness was graded into 4 stages - stage I - stupor, stage II - light coma, stage III - deep coma and stage IV - patient flaccid and apneic.

The child's posture was examined and was described as normal, decorticate or decerebrate.

Speech and gait of the child were observed, if possible. Sign of meningeal irritation such as neck rigidity, kernig's sign and brudzinski's sign were elicited. Fundus examination was carried out in each case.

Cranial nerves specially optic nerve, occulomotor nerve, trochlear nerve, abducent nerve and facial nerves were examined in detail.

Each group of muscles was examined for bulk, tone, coordination and involuntary movements.

Perception to fine and coarse touch, pain, temperature, position and joint sense, vibration and cortical sensations were evaluated, whenever possible.

Superficial reflexes such as corneal, conjunctival, pupillary, abdominal, cremastric and planters and deep tendon reflexes such as biceps, triceps, supinator, knee and ankle jerks were examined in detail. Besides these, the child was examined for the presence of cerebellar and extrapyrimidal signs.

Thorough systemic examination was made to detect any abnormality in cardio-vascular, digestive and respiratory systems.

Laboratory investigations viz. haemoglobin, leucocyte count (total and differential), erythrocyte sedimentation rate, CSF examination for tension, colour, coagulum, protein, sugar, chloride and cells was carried out routinely in each and every case. Grams staining, culture and sensitivity of the CSF were done in each case. Radiological and other relevant investigations were performed if necessary.

Blood was collected by venepuncture. CSF was collected after doing lumbar puncture. Samples were stored at $4^{\circ}C$ in refrigerator. Magnesium and calcium levels were estimated within 48 hours of sample collection. All the glasswares were stored in chromic acid cleaning solution and rinsed just before use and were used wet.

I - Determination of serum and CSF magnesium level.

Serum and CSF magnesium were determined by colorimetric method using titan yellow reagent, described by Neill and Neely (1956).

Principle - Titan yellow gives a red colour with magnesium. Neill and Neely modified earlier methods by using gum ghatti as the colour stabilizer and including calcium in the standard. Calcium intensifies the colour

so this allows for the effect of calcium present in the serum.

Reagents :

1. Sodium tungstate (10%) :-

10 gm of sodium tungstate was dissolved in 100 ml of distilled water to prepare 10% solution.

2. Gum ghatti (0.1%) :-

0.1 gm of powdered gum ghatti in a muslin bag was suspended in 100 ml of distilled water for 24 hours to prepare 0.1% gum ghatti.

3. Sulphuric acid (2/3 N) :-

18 ml of concentrated sulphuric acid was added carefully, with mixing, to about 90 ml of distilled water. Then the volume was made to 100 ml to prepare 2/3 N sulphuric acid.

4. Titan Yellow (0.05%) :-

0.1 gm of powdered dye was dissolved in 200 ml of distilled water to prepare 0.05% solution of titan yellow.

5. Sodium hydroxide (4 N) :-

1.6 gm of sodium hydroxide was dissolved in 100 ml of distilled water to make 4 N sodium hydroxide.

6. Stock standard solution :-

8.45 gm of $Mgcl_2$, $6H_2O$ was dissolved in distilled water and made upto a litre.

7. Standard solution for use (5 ug/ml) :-

1 ml of stock solution was diluted in 200 ml with distilled water. This contains 5 micrograms of magnesium per ml.

8. Calcium chloride solution (0.05 mg/ml) :-

13.88 mg of calcium chloride was dissolved in distilled water and made upto 100 ml. This solution contains 0.05 mg calcium per ml.

Procedure :-

1 ml of serum was diluted with 5 ml of distilled water and proteins were precipitated by adding 2 ml of 10% sodium tungstate and 2 ml of 2/3 N sulphuric acid. This was centrifuged for 10 minutes at 3000 revolutions per minute. 5 ml of the supernatant fluid was taken in a test tube. To this were added in turn 1 ml of distilled water, 1 ml of gum ghatti, 1 ml of 0.05 percent titan yellow and 2 ml of 4 N sodium hydroxide.

At the same time 1 ml of calcium chloride and 5 ml of distilled water was pipetted in a test tube marked as blank, and 1 ml of calcium chloride and 2.5 ml

of the working standard and 2.5 ml of distilled water were kept in another test tube marked as standard. To these test tubes were also added in turn 1 ml of distilled water, 1 ml of gum ghatti, 1 ml of 0.05 percent titan yellow and 2 ml of 4 N sodium hydroxide.

Standard and unknown were read in colorimeter against the blank, using a green filter (520 millimicrons).

Calculation :-

Mg. magnesium per 100 ml serum

$$= \frac{\text{Reading of unknown}}{\text{Reading of standard}} \times 2.5$$

II - Determination of serum and CSF calcium level :

Serum and CSF calcium was determined by Trinders technique (1960), using calcium kit supplied by Span Diagnostics, Private Limited, Udhna (Surat), India.

Principle :- Calcium present in the serum or CSF is precipitated with naphthal hydroxamic acid. The precipitate is then dissolved by the addition of EDTA reagent. This solution, on addition of color reagent, forms a colour complex which can be measured colorimetrically. Only a small excess of napthal hydroxamic acid, as a precipitating agent, is required for precipitating calcium and hence the precipitate does not require washing.

Reagents :

1. Calcium reagent :-

250 mg of naphthal hydroxamic acid was dissolved by warming in 100 ml of water containing 5 ml of ethanolamine and 2 gm of tartaric acid. To this was added 9 gm of sodium chloride dissolved in 500 ml of water and then diluted to 1 litre with water. If a precipitate was formed, it was filtered through a whatman No. 40 or 43 paper.

2. EDTA Solution :-

2 gm of disodium ethylenediamine tetra acetic acid was dissolved to 1 litre of 0.1 N sodium hydroxide.

3. Colour reagent :-

60 gm of ferric nitrate ($Fe(NO_3)_3$ 9 H_2O) was dissolved in 500 ml of water. To this was added 15 ml of concentrated nitric acid and was diluted to 1 litre with water.

Calcium standard :-

125 mg of dry calcium carbonate was dissolved in 40 ml of 0.1 N hydrochloric acid and was diluted to 500 ml with distilled water. This contained 5 mEq of calcium per litre.

Procedure :

Test :- 0.2 ml of serum was pipetted into a centrifuge tube. To this was added 5 ml of calcium reagent and mixed.

Standard :- 0.2 ml of calcium standard was pipetted into a centrifuge tube. To this was added 5 ml of calcium reagent and mixed.

Blank :-

5 ml of calcium reagent was taken in a centrifuge tube. These tubes were allowed to stand for 30 minutes at room temperature and then centrifuged at 3000 - 4000 revolutions per minute for 10 minutes. The supernatant was decanted by slowly inverting the tubes and placing them inverted for 5 minutes on filter paper to drain completely.

1 ml of EDTA solution was added to each test tube. Each test tube was shaken well to suspend the precipitate. The mouth of each tube was covered with an aluminium cap and kept in boiling water bath for 10 minutes with occasional mixing to dissolve the precipitate completely. Then the tubes were allowed to cool and 3 ml of colour reagent was added to each tube and mixed well.

The optical densities of test (T), standard (S) and Blank (B) were measured at 450 nm or using blue filter against distilled water as reference blank to set zero.

Calculations :-

$$\text{Calcium in mEq/litre} = \frac{(T) - (B)}{(S) - (B)} \times 5$$

OBSERVATIONS

OBSERVATIONS

A study to assess the concurrent changes in serum and cerebrospinal fluid (CSF) calcium and magnesium in neurological disorders was carried out in 40 children (Birth to 12 years age) at M.L.B. Medical College, Jhansi, between May 1982 and March 1983. Besides serum and CSF calcium and magnesium, various clinical features were noted, routine blood investigations and CSF cytological and biochemical examination were done in each case. A control group, comprising 8 age matched children not manifesting any neurological disorder, was also studied for comparative evaluation of serum and CSF calcium and magnesium and CSF cytological and biochemical values. Age and sex distribution, of control subjects and those who had different neurological disorders is shown in table 1.

Out of 40 cases with neurological disorders 15 cases had tuberculous meningitis, 7 had pyogenic meningitis and 9 cases each were suffering from encephalitis and grand mal epilepsy.

Table - 1

Age & sex distribution

Group	Total No.of cases	Sex		No. of cases in different age groups									
		M	F	(0-1)		(1-3)		(3-6)		(6-9)		(9-12)	
				M	F	M	F	M	F	M	F	M	F
1. Control	8	4	4	1	-	1	1	1	1	1	1	-	1
2. Tuberculous meningitis	15	10	5	3	-	3	2	4	1	1	-	1	-
3. Pyogenic meningitis	7	4	3	3	1	1	-	-	1	-	-	1	-
4. Encephalitis	9	3	6	-	-	-	-	1	-	2	5	-	1
5. Epilepsy	9	7	2	-	-	-	-	1	1	3	1	3	-
Total	48	28	20	7	1	5	3	7	4	7	7	5	2

VACCINATION HISTORY -

The immunization status of the control group and those having neurological disorders is shown in table 2. Out of the total 48 cases, 10 were immunized for smallpox, 3 for tuberculosis, 3 for polio and 2 for DPT. It is evident from the table that out of 15 tuberculous meningitis cases only one had been immunized for B.C.G.

Table - 2

Vaccination history

Groups	No.of cases	Smallpox	B.C.G.	D.P.T.	Polio
Control	8	3	1	2	2
Tuberculous meningitis	15	2	1	-	1
Pyogenic meningitis	7	1	-	-	-
Encephalitis	9	3	-	-	-
Epilepsy	9	1	1	-	-
Total	48	10	3	2	3

FAMILY HISTORY :

Family history of tuberculosis was positive in 7 cases of tuberculous meningitis. Also, one case each

of septic meningitis and epilepsy, family history of tuberculosis was present. None of the cases in control group and those suffering from encephalitis had family history of tuberculous infection.

ANTHROPOMETRIC MEASUREMENTS :

Mean weight and head circumference, in control subjects and those suffering from tuberculous meningitis, pyogenic meningitis, encephalitis and epilepsy, has been shown in table 3.

Table - 3

Anthropometric profile on initial contact.

Groups	No.of cases	Weight (kg.) Mean ± S.D.	Head circumference (cms.) Mean ± S.D.
Control	8	11.6 ± 4.19	46.6 ± 2.77
Tuberculous meningitis	15	9.8 ± 3.80	45.4 ± 3.47
Pyogenic meningitis	7	10.0 ± 5.46	43.6 ± 5.13
Encephalitis	9	15.9 ± 2.15	48.0 ± 1.23
Epilepsy	9	18.7 ± 6.43	48.6 ± 2.03

The presenting symptoms in children suffering from tuberculous meningitis, acute bacterial meningitis and encephalitis have been shown in table 4.

Table - 4

History at the time of admission.

Symptoms	Tuberculous meningitis(%) n = 15	Pyogenic meningitis(%) n = 7	Encephalitis (%) n = 9
Fever	15 (100%)	7 (100%)	9 (100%)
Altered sensorium	12 (80.00%)	5 (71.42%)	9 (100%)
Convulsions	11 (73.33%)	5 (71.42%)	7 (77.77%)
Vomiting	10 (66.66%)	3 (42.85%)	7 (77.77%)
Headache	3 (20.00%)	1 (14.28%)	1 (11.11%)
Irritability	1 (6.66%)	2 (28.57%)	-
Weakness in any part of body	1 (6.66%)	-	-

As is seen from the table, important symptoms in each group were fever, vomiting, altered sensorium and convulsion.

Table 5 shows the level of consciousness at the time of admission in cases of tuberculous meningitis, acute bacterial meningitis and encephalitis. Out of 15, only 3 cases of tuberculous meningitis and

2 out of the 7 cases suffering from acute bacterial meningitis were conscious, while no case of encephalitis was conscious at the time of admission.

Table - 5

Level of consciousness at initial contact.

Group	No loss of consciousness	Grades of coma				Total
		I	II	III	IV	
Tuberculous meningitis	3	1	4	6	1	15
Pyogenic meningitis	2	1	1	3	-	7
Encephalitis	-	-	4	4	1	9

Various neurological signs at the time of admission have been depicted in table 6.

It is evident from the table that in tuberculous meningitis, out of the 15 cases, 4 manifested with hemiparesis while 5 had quadriparesis. Extrapyramidal involvement in the form of tremors and choreoathetoid movements were noticed in one and two cases respectively. Facial nerve involvement occurred in 2 cases, whereas only one case had 3rd nerve palsy. In pyogenic meningitis, incidence of neurological complications were less, one case each presented with hemiparesis, quadriparesis and

facial nerve involvement. In encephalitis 2 cases presented with quadriparesis and one had tremors.

Table - 6

Signs at the time of admission.

Signs	Tuberculous meningitis (n=15)	Pyogenic meningitis (n=7)	Encephalitis (n=9)
VII Cranial nerve palsy	2	1	-
III Cranial nerve palsy	1	-	-
Other cranial nerves palsies	-	-	-
Hemiparesis	4	1	-
Monoparesis	-	-	-
Quadriparesis	5	1	2
Tremors	1	-	1
Choreoathetoid movements	2	-	-

Table 7 shows fundus changes in the eyes at initial contact. It is evident from the table that in tuberculous meningitis 33.33% cases had primary optic atrophy, 6.66% cases had secondary optic atrophy, 13.33% cases had papilloedema and 20% had pallor of the disc. In pyogenic meningitis, in contrast to tuberculous meningitis, 28.57% cases had evidence of papilloedema,

14.28% had pallor of disc, but none showed evidence of primary or secondary optic atrophy. In cases suffering from encephalitis, none had primary or secondary optic atrophy. However, 22.22% of the cases had papilloedema and 11.11% had pallor of disc.

Table - 7

Fundus changes at initial contact.

Group	No changes	Pallor of disc	Primary optic atrophy	Secondary optic atrophy	Papilloedema	Total
Tuberculous meningitis	4 (26.66%)	3 (20.00%)	5 (33.33%)	1 (6.66%)	2 (13.33%)	15
Pyogenic meningitis	4 (57.14%)	1 (14.28%)	-	-	2 (28.57%)	7
Encephalitis	6 (66.66%)	1 (11.11%)	-	-	2 (22.22%)	9

HAEMATOLOGICAL VALUES :

Table 8 shows mean haemoglobin and ESR values in all the study groups. There was no statistically significant difference in the haemoglobin and ESR values in various study groups.

Table - 8

Haematological values in different groups.

Group	No.of cases	Hb.(gm%) Mean ± S.D.	ESR (mm for 1st hr.) Mean ± S.D.
Control	8	9.3 ± 1.01	18.2 ± 14.26
Tuberculous meningitis	15	8.4 ± 1.04	20.5 ± 13.59
Pyogenic meningitis	7	8.6 ± 0.90	25.0 ± 14.62
Encephalitis	9	8.1 ± 1.58	30.1 ± 14.26
Epilepsy	9	9.8 ± 1.11	24.1 ± 17.98

SERUM AND CSF CALCIUM AND MAGNESIUM :

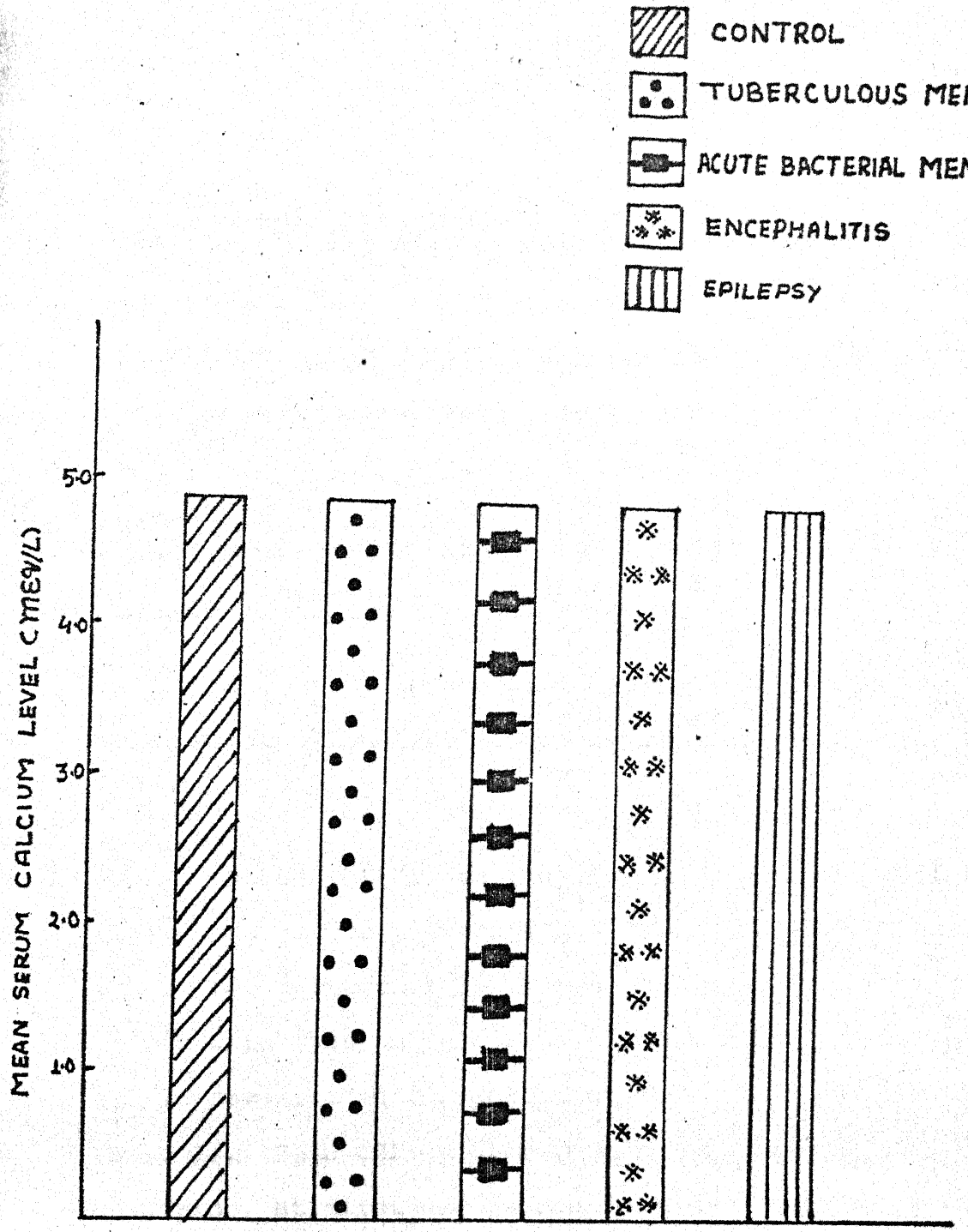
Controls :-

Table 9 shows mean serum and CSF calcium and magnesium levels in control subjects.

Table - 9

Serum & CSF calcium & magnesium in controls.

		Mean ± S.D. (n=8) (mEq/l)	t	P
Calcium	Serum	4.9 ± 0.22	29.279	< 0.001
	CSF	2.3 ± 0.12		
Magnesium	Serum	2.2 ± 0.22	4.158	< 0.001
	CSF	2.6 ± 0.16		



BAR DIAGRAM SHOWING MEAN SERUM CALCIUM LEVELS IN CONTROL AND VARIOUS NEUROLOGICAL DISORDERS AT INITIAL CONTACT.

fig.-1

It is evident from the table that in control subjects mean serum calcium level (mEq/l) was higher (4.9 ± 0.22) than that observed in CSF (2.3 ± 0.12), difference between the two being statistically significant ($P < 0.001$). Contrarily, it was found that the magnesium levels (mEq/l) were higher in CSF (2.6 ± 0.16) than in serum (2.2 ± 0.22), difference again being statistically significant ($P < 0.001$).

Tuberculous meningitis :

Serum and CSF calcium and magnesium values in tuberculous meningitis cases has been shown in table 10.

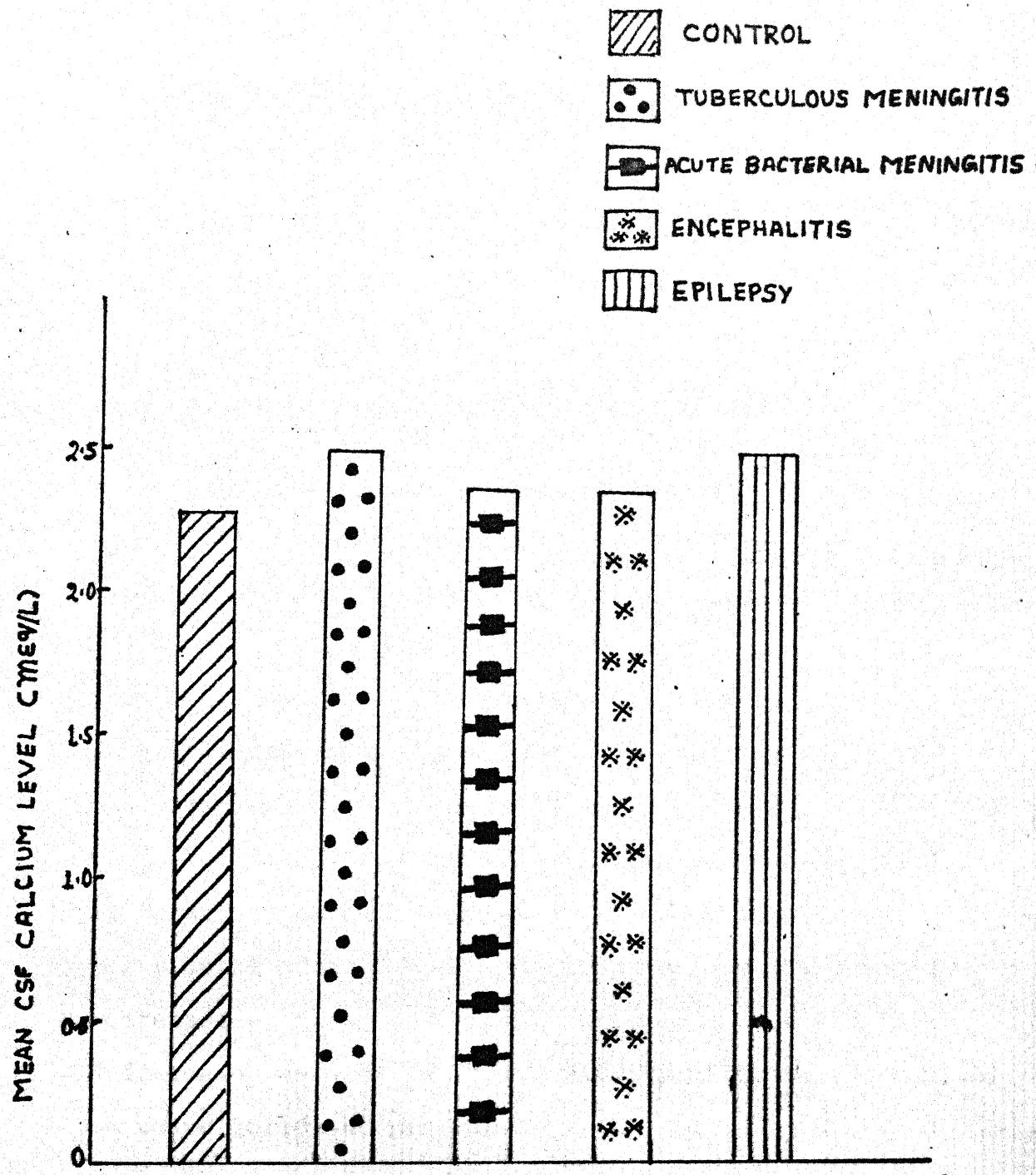
It is evident from the table that the mean serum calcium (mEq/l) at the time of admission, at first and second follow-up were 4.9 ± 0.24, 5.0 ± 0.16 and 5.0 ± 0.20 respectively. A comparison of these mean values with those obtained in control subjects (4.9 ± 0.22 mEq/l) revealed an insignificant difference ($P > 0.05$) (Fig. 1). Mean CSF calcium (mEq/l) at the time of admission, at first and second follow-up were 2.5 ± 0.13, 2.5 ± 0.09 and 2.4 ± 0.04 respectively. On comparing these mean values to those obtained in control subjects (2.3 ± 0.12 mEq/l), the differences were found to be significant at the time of admission and at first follow-up ($P < 0.01$ and < 0.001 respectively), while the difference was insignificant at second follow-up

Table - 10

Serum and CSF calcium and magnesium in Tuberculous Meningitis.

		Control (n = 8) Mean±S.D. (mEq/l)	At the time of admission (n = 15) Mean±S.D. (mEq/l)	(Control vs admission) t	P	1st follow-up (n=10) Mean±S.D. (mEq/l)	(Control vs 1st follow-up) t	P	2nd follow-up (n=3) Mean±S.D. (mEq/l)	(Control vs 2nd follow-up) t	P
Calcium	Serum	4.9±0.22	4.9±0.24	0	>0.05	5.0±0.16	1.118	>0.05	5.0±0.20	0.685	>0.05
	CSF	2.3±0.12	2.5±0.13	3.602	<0.01	2.5±0.09	4.047	<0.001	2.4±0.04	1.374	>0.05
Magnesium	Serum	2.2±0.22	1.7±0.23	5.038	<0.001	1.9±0.22	2.875	<0.05	1.9±0.40	1.638	>0.05
	CSF	2.6±0.16	1.9±0.21	8.208	<0.001	2.1±0.20	5.56	<0.001	2.1±0.40	3.136	<0.05

	Comparison of mean values at admission and first follow-up t	P	Comparison of mean values at admission and second follow-up t	P
S. Calcium	0.271	> 0.05	0.1755	> 0.05
CSF Calcium	0	> 0.05	0.3249	> 0.05
S. Magnesium	0.5622	> 0.05	0.3626	> 0.05
CSF Magnesium	0.6158	> 0.05	0.3960	> 0.05



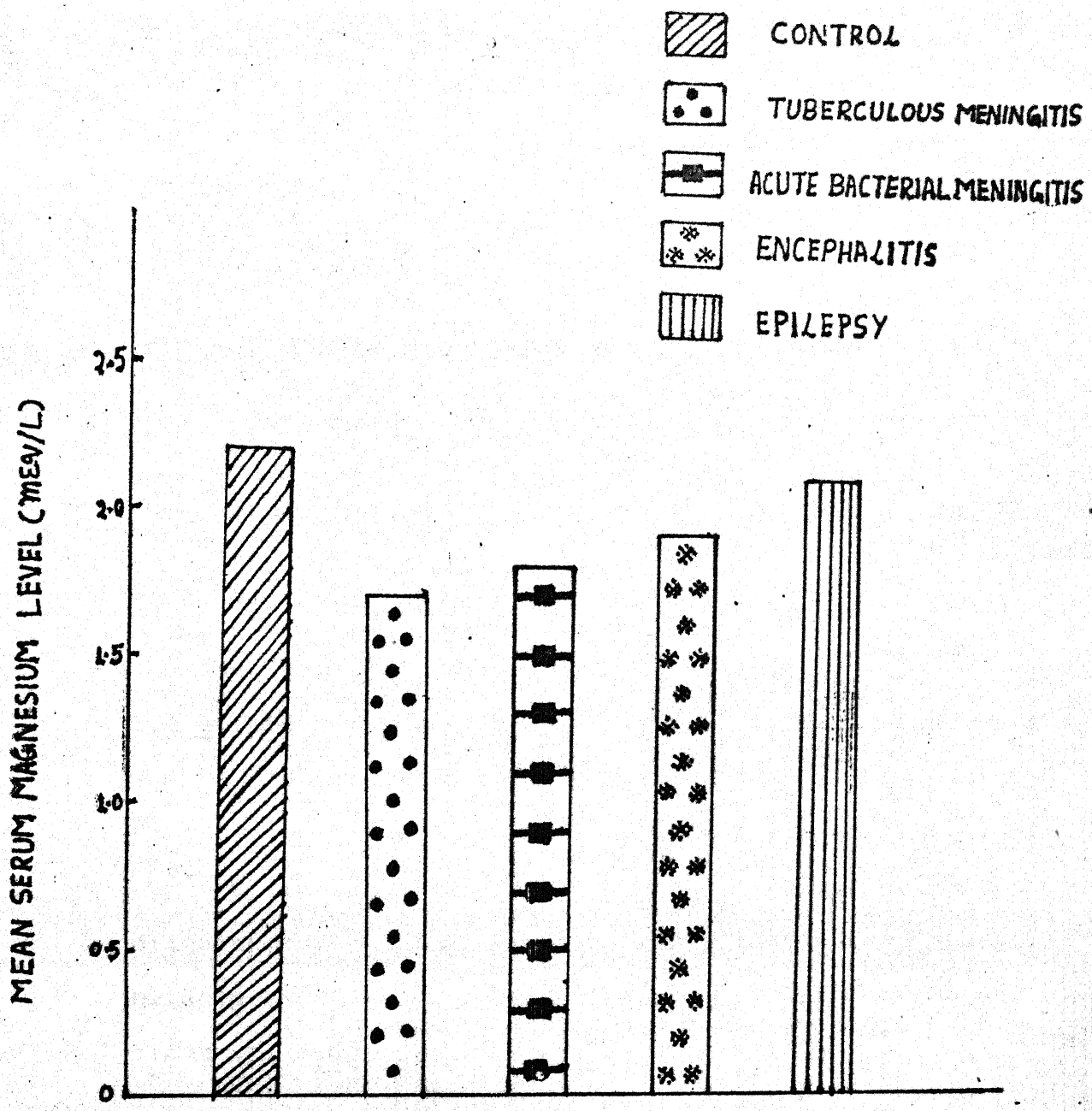
BAR DIAGRAM SHOWING MEAN CSF CALCIUM LEVELS IN CONTROLS AND VARIOUS NEUROLOGICAL DISORDERS AT INITIAL CONTACT

fig. 2

($P > 0.05$) (Fig. 2). Further, on comparing the mean serum and CSF calcium at first and second follow-up with the mean values at initial contact, no significant difference could be found ($P > 0.05$).

Further, the mean serum magnesium (mEq/l) values were found to be 1.7 ± 0.23, 1.9 ± 0.22 and 1.9 ± 0.40, at the time of admission, at first and second follow-up respectively. A comparison of these values with those in controls (2.2 ± 0.22 mEq/l) revealed that the values were significantly lower at the time of admission ($P < 0.001$) and at first follow-up ($P < 0.05$). Although the mean value at second follow-up was lower than that seen in controls, the difference was statistically insignificant ($P > 0.05$) (Fig. 3 & 4). On comparing mean serum magnesium values, at first and second follow-up with the mean value at the time of admission, serum magnesium was found to have increased at first and second follow-up. However, differences were not statistically significant ($P > 0.05$) at these follow-up periods.

The mean CSF magnesium (mEq/l) values were found to be 1.9 ± 0.21, 2.1 ± 0.20 and 2.1 ± 0.40, at the time of admission, at first and second follow-up respectively. A comparison of these values with those of mean CSF magnesium value in controls (2.6 ± 0.16 mEq/l)



BAR DIAGRAM SHOWING MEAN SERUM MAGNESIUM LEVELS IN CONTROL AND VARIOUS NEUROLOGICAL DISORDERS AT INITIAL CONTACT.

Fig. 3

showed a significant lowering ($P < 0.001$, < 0.001 and < 0.05 respectively). Similar to the serum magnesium and CSF magnesium also increased at first and second follow-up and the differences were statistically insignificant ($P > 0.05$) (Fig. 5 & 6).

Acute bacterial meningitis :

The mean serum and CSF calcium and magnesium levels in acute bacterial meningitis have been shown in table 11.

It is evident from the table that mean serum calcium (mEq/l) values were 4.9 ± 0.16, 5.0 ± 0.07 and 5.1 ± 0.06, at the time of admission, at first follow-up and second follow-up respectively, revealing an insignificant differences in comparison to controls ($P > 0.05$) (Fig. 1). Also, there was an insignificant difference ($P > 0.05$) in the mean serum calcium values, between those obtained at the time of admission and at first and second follow-up.

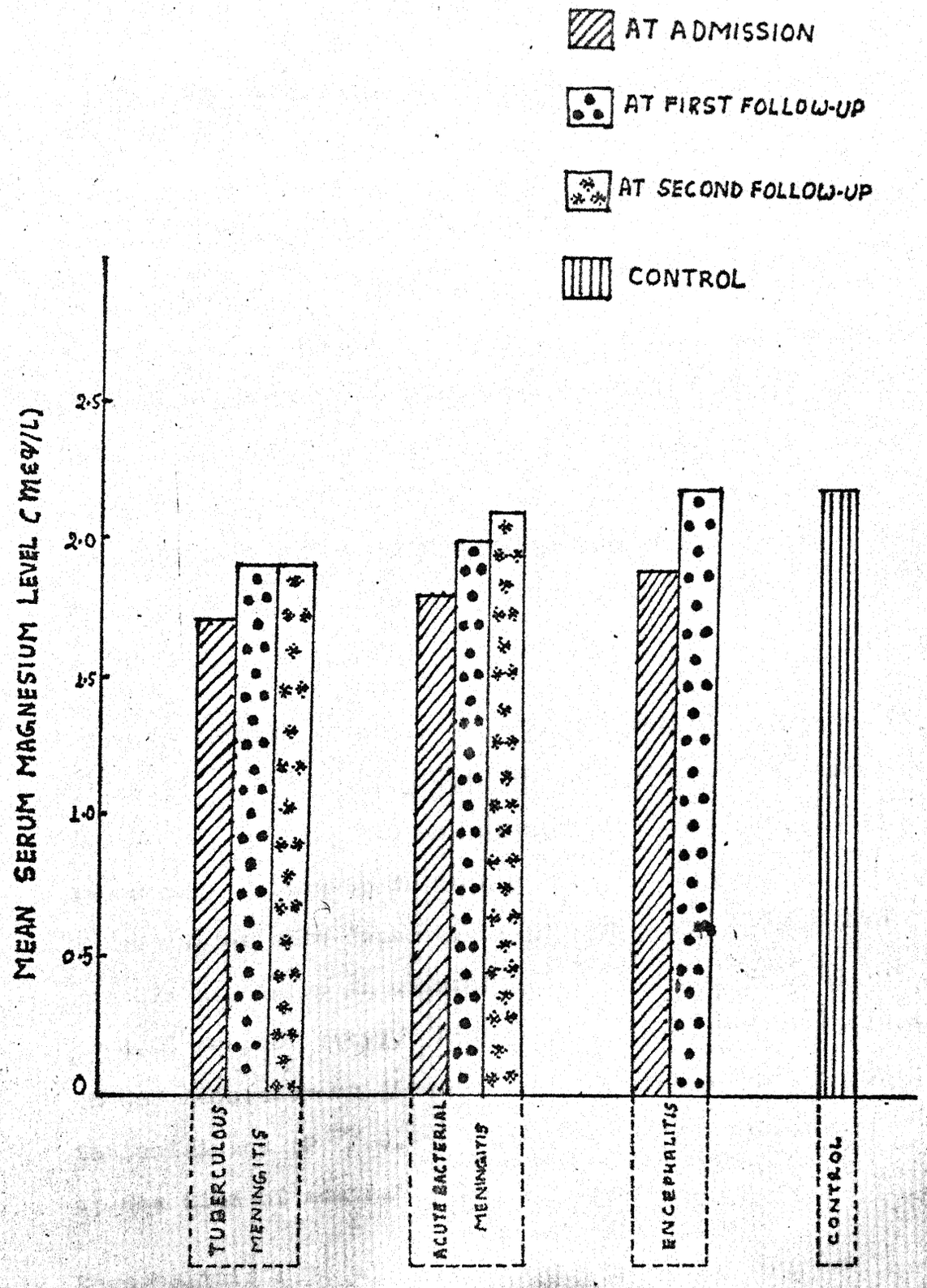
Similarly, the mean CSF calcium (mEq/l) levels were higher, though insignificant ($P > 0.05$), at the time of admission and at first and second follow-up, in comparison to controls (Fig. 2). Again, there were statistically insignificant ($P > 0.05$) differences in the mean CSF calcium levels at the time of admission and at first and second follow-up.

Table - 11

Serum & CSF calcium & magnesium in Pyogenic Meningitis.

		Control (n=8) Mean±S.D. (mEq/l)	At the time of admission (n=7) Mean±S.D. (mEq/l)	(Control vs admission t	P	1st follow-up (n=4) Mean±S.D. (mEq/l)	(Control vs. 1st follow-up t	P	2nd follow-up (n=2) Mean±S.D. (mEq/l)	(Control vs 2nd follow-up t	P
Calcium	Serum	4.9±0.22	4.9±0.16	0	>0.05	5.0±0.07	0.869	>0.05	5.1±0.06	1.223	>0.05
	CSF	2.3±0.12	2.4±0.07	1.930	>0.05	2.4±0.08	1.490	>0.05	2.4±0.11	1.065	>0.05
Magnesium	Serum	2.2±0.22	1.8±0.13	4.201	<0.01	2.0±0.24	1.444	>0.05	2.1±0.32	0.539	>0.05
	CSF	2.6±0.16	1.9±0.09	10.217	<0.001	2.2±0.40	2.543	<0.05	2.2±0.40	2.456	<0.05

	Comparison of mean values at initial contact and first follow-up t	P	Comparison of mean values at initial contact and second follow-up t	P
S. Calcium	0.4049	> 0.05	0.635	> 0.05
CSF Calcium	0	> 0.05	0	> 0.05
S. Magnesium	0.919	> 0.05	1.099	> 0.05
CSF Magnesium	1.499	> 0.05	1.40	> 0.05



BAR DIAGRAM SHOWING CHANGES IN MEAN SERUM MAGNESIUM LEVELS AT FOLLOW-UP IN ACUTE NEUROLOGICAL DISORDERS.

Fig. - 4

The mean serum magnesium (mEq/l) levels were 1.8 ± 0.13, 2.0 ± 0.24 and 2.1 ± 0.32, at the time of admission, at first and 2nd follow-up respectively. On statistical analysis the mean serum magnesium was significantly lower ($P < 0.01$) at the time of admission as compared to values obtained in controls. Although, mean serum magnesium was also low at first and second follow-up, the difference with the controls were insignificant ($P > 0.05$). Also there were statistically insignificant ($P > 0.05$) differences in the serum magnesium at first and second follow-up in comparison to serum magnesium at admission (Fig. 3 & 4).

Further, mean CSF magnesium (mEq/l) was found to be 1.9 ± 0.09, 2.2 ± 0.40 and 2.2 ± 0.40, in cases of pyogenic meningitis at the time of admission, first and second follow-up respectively. Statistically, these values were found to be significantly lower than the CSF magnesium in controls ($P < 0.001$, < 0.05 and < 0.05 respectively). Like serum magnesium, differences in CSF magnesium at first and second follow-up were also insignificant ($P > 0.05$) when compared to mean value at the time of admission (Fig. 5 & 6).

Encephalitis :

Serum and CSF calcium and magnesium levels in encephalitis have been shown in table 12.

Table - 12

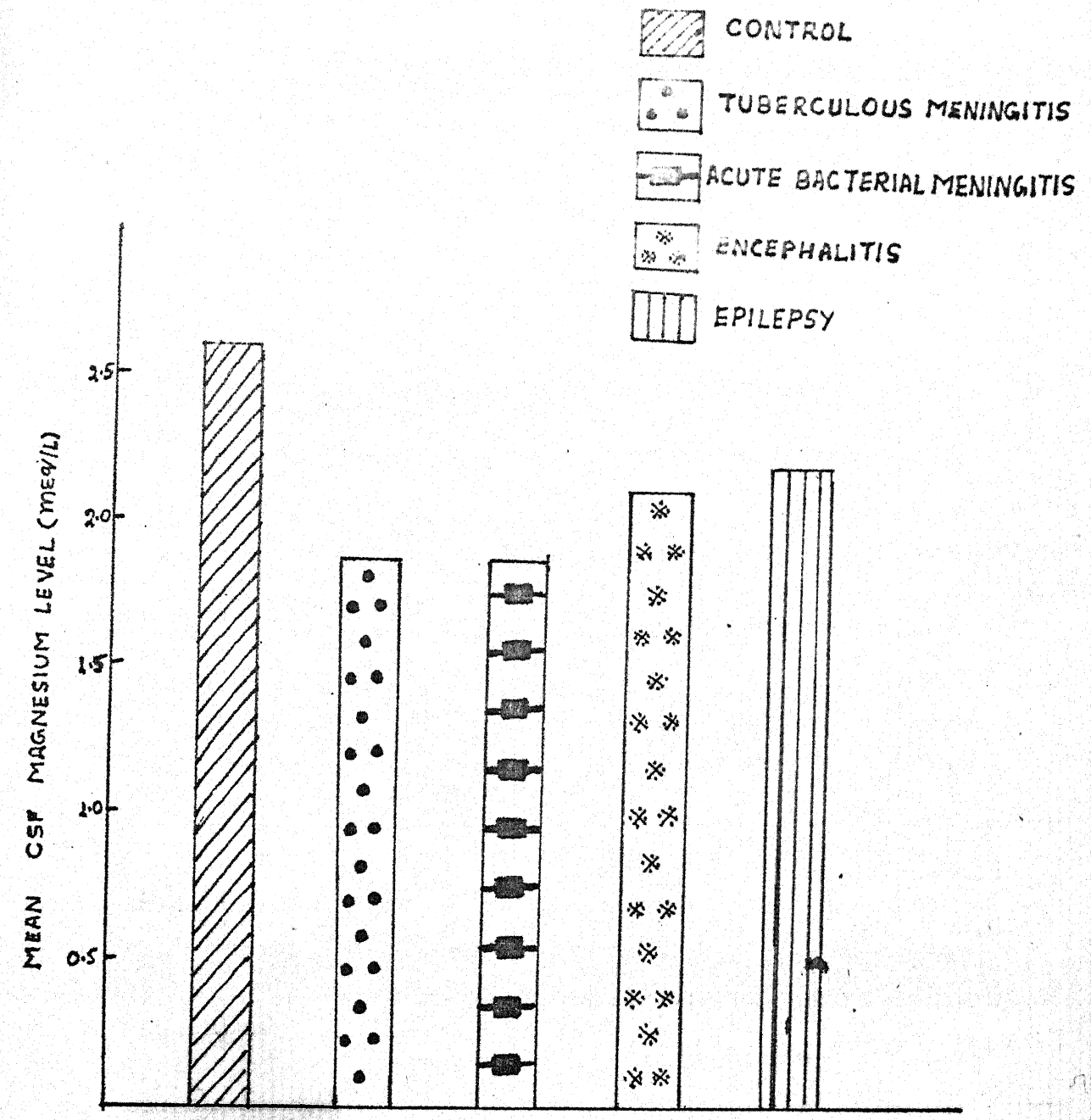
Serum & CSF calcium & magnesium levels in Encephalitis.

		Control (n=8) Mean±S.D. (mEq/l)	At the time of admission (n=9) Mean±S.D. (mEq/l)	t	P	1st follow-up (n=7) Mean±S.D. (mEq/l)	t	P	Comparison between mean values at admission and first follow-up t	P
Calcium	Serum	4.9±0.22	4.9±0.20	0	>0.05	4.9±0.16	0	>0.05	0	>0.05
	CSF	2.3±0.12	2.4±0.09	1.958	>0.05	2.4±0.14	0.583	>0.05	0	>0.05
Magnesium	Serum	2.2±0.22	1.9±0.22	2.946	<0.01	2.2±0.07	0	>0.05	1.049	>0.05
	CSF	2.6±0.16	2.1±0.09	8.071	<0.001	2.4±0.12	2.702	<0.05	2.234	<0.05

It is evident from the table that there was a statistically insignificant difference ($P > 0.05$) between the mean serum and CSF calcium at the time of admission and at the first follow-up in comparison to controls (Fig. 1 & 2). Also, there was a statistically insignificant ($P > 0.05$) difference between serum and CSF calcium values at the time of admission and first follow-up.

Mean values of serum magnesium (mEq/l) were 1.9 ± 0.22 and 2.2 ± 0.07 in encephalitis at the time of admission and at first follow-up respectively. A comparison of these mean values to those obtained in controls (2.2 ± 0.22 mEq/l) revealed that the serum magnesium was significantly lower at the time of admission ($P < 0.01$) but no significant difference was found at the time of first follow-up ($P > 0.05$). Further, it was observed that although there was a rise in serum magnesium at first follow-up in comparison to serum magnesium at the time of admission, the rise was not statistically significant ($P > 0.05$) (Fig. 3 & 4).

Mean CSF magnesium (mEq/l) was 2.1 ± 0.09 and 2.4 ± 0.12, at the time of admission and at first follow-up respectively. A comparison of these mean values to those obtained in controls (2.6 ± 0.16 mEq/l) revealed significantly low values ($P < 0.001$ and < 0.05 respectively) in children suffering from encephalitis.



BAR DIAGRAM SHOWING MEAN CSF MAGNESIUM LEVELS IN CONTROL AND VARIOUS NEUROLOGICAL DISORDERS AT INITIAL CONTACT.

Fig. 5

There was also a significant difference in mean CSF magnesium levels between the time of admission and first follow-up ($P < 0.05$), being higher later on (Fig. 5 & 6).

Epilepsy :

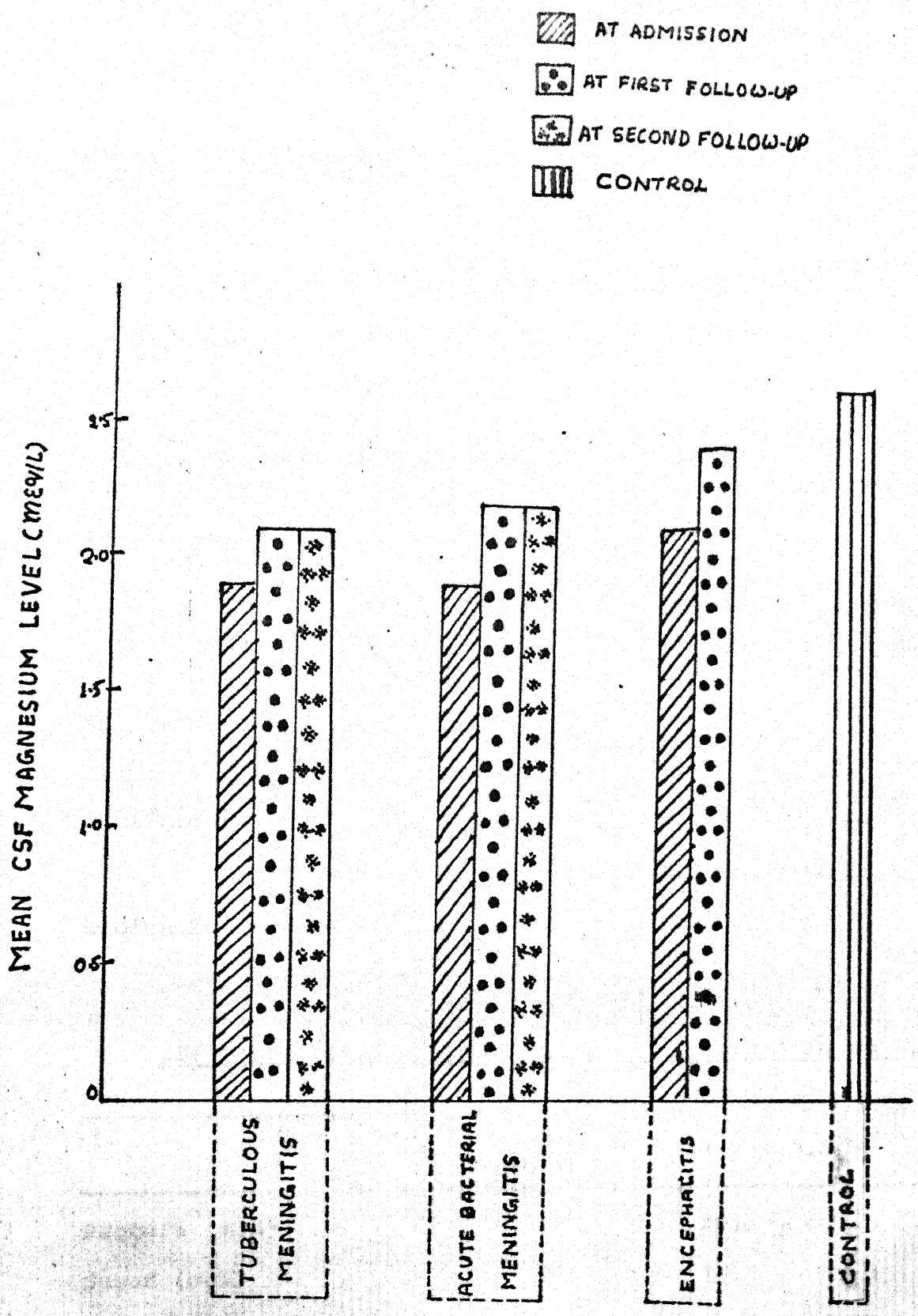
The mean serum and CSF calcium and magnesium levels in epilepsy have been shown in table 13.

Table - 13

Serum & CSF calcium & magnesium in Epilepsy.

		Controls (n=8) Mean±S.D. (mEq/l)	Epilepsy (n=9) Mean±S.D. (mEq/l)	t	P
Calcium	Serum	4.9±0.22	4.9±0.26	0	> 0.05
	CSF	2.3±0.12	2.5±0.18	1.198	> 0.05
Magnesium	Serum	2.2±0.22	2.1±0.17	0.346	> 0.05
	CSF	2.6±0.16	2.2 ±0.14	2.363	< 0.05

Mean serum and CSF calcium (mEq/l) levels were found to be 4.9 ± 0.26 and 2.5 ± 0.18 respectively at the time of admission. On comparing mean serum calcium levels in control subjects with those obtained in epileptic patients, no difference was found (Fig. 1 & 2). Calcium level in CSF was higher in epileptic children as compared



BAR DIAGRAM SHOWING CHANGES IN MEAN CSF MAGNESIUM LEVELS AT FOLLOW-UP IN ACUTE NEUROLOGICAL DISORDERS

Fig - 6

to those obtained in control subjects. However, this difference was statistically insignificant ($P > 0.05$).

Further, the mean serum and CSF magnesium (mEq/l) levels were found to be 2.1 ± 0.17 and 2.2 ± 0.14 respectively in epileptic patients. A comparison of these mean values to those obtained in control subjects revealed lower levels in epilepsy cases. The difference, between comparable groups, were statistically insignificant in serum ($P > 0.05$) but significant in CSF ($P < 0.05$) (Fig. 3 & 5).

CYTOLOGICAL AND BIOCHEMICAL ANALYSIS OF CSF :

Controls :

Table 14 shows the mean CSF cytological and biochemical values in controls.

Table - 14

CSF cytological & other biochemical values in controls.

	No.of cases	Mean ± S.D.
Protein (mg%)	8	24.7 ± 4.80
Sugar (mg%)	6	54.5 ± 26.13
Chlorides (mg%)	8	707.5 ± 12.99
Cells (/cubic mm)	8	< 5

Mean CSF protein, sugar and chloride levels (mg/dl) were 24.7 ± 4.80, 54.5 ± 26.13 and 707.5 ± 12.99 respectively in control subjects. Mean cell count was less than 5 cells/cubic mm in this group.

Tuberculous Meningitis :

The mean CSF cytological and biochemical values in tuberculous meningitis have been shown in table 15.

Table - 15

CSF cytological & biochemical values in tuberculous meningitis.

	At the time of admission Mean ± S.D.	1st follow-up Mean ± S.D.	2nd follow-up Mean ± S.D.
Protein (mg%)	331.1±475.37 n=14	180.0±110.81 n=10	109.3±15.08 n=3
Sugar (mg%)	28.8±24.07 n=13	30.0±5.90 n=7	31.5±3.5 n=2
Chlorides (mg%)	643.9±43.51 n=14	632.0±55.46 n=10	676.7±20.55 n=3
Cells (/cubic mm)	192.5±208.31 n=14	155.5±199.19 n=10	55.0±22.73 n=3

Mean CSF protein, sugar and chloride content (mg/dl), at the time of admission, were 333.1±475.37, 28.8 ± 24.07 and 643.9 ± 43.51 respectively. Mean cell

count was 192.5 ± 208.31 at the time of admission. While, there was a lowering in mean CSF protein and cell values at first and second follow-up in tuberculous patients, mean sugar and chloride values showed increased values in these cases.

Acute bacterial meningitis :

Mean CSF cytological and biochemical changes in acute bacterial meningitis have been shown in table 16.

Table - 16

CSF cytological & other biochemical values in pyogenic meningitis.

	At the time of admission Mean ± S.D.	First follow-up Mean ± S.D.	Second follow-up Mean ± S.D.
Protein (mg%)	587.1±988.10 n=7	672.5±1055.14 n=4	145.0±105.0 n=2
Sugar (mg%)	8.9±5.77 n=7	30.0 n=1	-
Chlorides (mg%)	661.4±70.60 n=7	690.0±30.0 n=4	710.0±10.0 n=2
Cells (/cubic mm)	3025.0±4111.72 n=7	167.2±250.17 n=4	52.5±47.5 n=2

The mean CSF protein, sugar and chloride levels (mg/dl), at the time of admission, were 587.1 ± 998.10, 8.9 ± 5.77 and 661.4 ± 70.60 respectively and the mean cell count was 3025.0 ± 4111.72 cells/cubic mm. An increase in mean CSF sugar and chloride and a decrease in mean CSF protein and cell counts was observed at first and second follow-up, in these cases.

Encephalitis :

Table 17 shows the mean CSF cytological and biochemical values in encephalitis.

Table - 17

CSF cytological & biochemical values in Encephalitis.

	At the time of admission Mean ± S.D.	First follow-up Mean ± S.D.
Protein (mg%)	34.7±17.66 n=9	27.3±11.22 n=7
Sugar (mg%)	62.4±17.68 n=5	46.7±10.33 n=4
Chloride (mg%)	702.2±41.57 n=9	715.7±21.28 n=7
Cells (/cubic mm)	28.3±38.00 n=9	12.1±11.60 n=7

It is evident from the table that the mean CSF protein, sugar and chloride contents at the time of admission were 34.7 ± 17.66, 62.4 ± 17.68 and 702.2 ± 41.57 respectively and the corresponding values at first follow-up were 27.3 ± 11.22, 46.7 ± 10.33 and 715.7 ± 21.28 respectively. Further, the mean cell count in CSF were 28.3 ± 38.00 and 12.1 ± 11.60 at the time of admission and first follow-up respectively.

Epilepsy :

Mean CSF cytological and biochemical values in epilepsy have been shown in table 18. Mean CSF protein, sugar and chloride (mg/dl) were observed to be 20.9 ± 5.34, 46.2 ± 17.79 and 731.1 ± 30.35 respectively, while the mean CSF cell count was less than 5 cells/cubic mm at the time of admission.

Table - 18

CSF cytological & biochemical values in Epilepsy at admission.

	n	Mean ± S.D.
Protein (mg%)	9	20.9 ± 5.34
Sugar (mg%)	4	46.2 ± 17.79
Chlorides (mg%)	9	731.1 ± 30.35
Cells (/cubic mm)	9	< 5

Table 19 depicts the outcome of cases in tuberculous meningitis, pyogenic meningitis and encephalitis.

Table - 19

Outcome of cases.

Group	Improved	Improved with sequelae	Left against medical advice	Absconded	Expired	Total
Tuberculous meningitis	4	1	3	2	5	15
Pyogenic meningitis	3	-	1	-	3	7
Encephalitis	6	-	1	-	2	9

D I S C U S S I O N

DISCUSSION

Present work was carried to study the serum and CSF calcium and magnesium in 40 children (birth to 12 years age) suffering from various acute neurological disorders and in 8 age matched children, not manifesting any neurological disorder, serving as control. This study was conducted at M.L.B. Medical College, Jhansi between May 1982 and March 1983.

Primary aim of our study was to evaluate serum and CSF calcium and magnesium in children suffering from tuberculous meningitis, acute bacterial meningitis, encephalitis and epilepsy and compare these values with those obtained in control cases. Besides evaluating the serum and CSF calcium and magnesium, various clinical features were noted and routine investigations like CSF cytology and biochemical examination were done in each case. It was also our endeavour to ascertain the possible inter-relationship between the clinical progress, following treatment, and the subsequent changes in serum and CSF calcium and magnesium levels. With this objective in view, serum and CSF calcium and magnesium levels, various clinical

features and CSF cytological and biochemical values were evaluated at the time of initial contact and in subsequent follow-up once or twice at 5 to 10 days interval each. Statistical analysis was done to derive means and standard deviations (SD). Mean values were compared using student 't' test and significances of difference were tested.

Out of the 40 cases suffering from neurological disorders, 15 had tuberculous meningitis, 7 had acute bacterial meningitis and 9 cases each were suffering from encephalitis and grand mal epilepsy. All the cases belonged to low socio-economic status.

Based on observations depicted in table 1 to 19, various inferences have been drawn and discussed under different headings.

Serum and CSF calcium in controls :

It is evident from the table 9 that in controls mean serum level of calcium was almost double (4.9 $\pm$ 0.22 mEq/l) than that observed in CSF (2.3 $\pm$ 0.12 mEq/l) and the difference was statistically significant ($P < 0.001$) (Fig. 1 & 2). These CSF and serum calcium values were found to be consistent with those observed by other workers viz. Misra et al (1973), Ahmad et al(1977), Kumar et al (1979) and Kumar et al (1981).

Serum and CSF magnesium in controls :

It is evident from the table 9, that in control cases contrary to calcium levels, magnesium levels were found to be higher in the CSF (2.6 ± 0.16 mEq/l) than in serum (2.2 ± 0.22 mEq/l) and the difference was statistically significant ($P < 0.001$) (Fig. 3 & 4). Similar magnesium values were observed by other workers viz. Cohen (1927), McCance and Watchron (1931), Chojnacki (1956), Misra et al (1973), Ahmad et al, (1977), Kumar et al (1981) and Praharaj et al (1982). Chojnacki (1956) suggested that the higher concentration of magnesium in CSF in comparison to that found in serum might be due to the contribution from magnesium rich central nervous system, through the perivascular and perineural spaces.

Serum and CSF calcium in tuberculous meningitis :

As seen from table 10, mean serum and CSF calcium levels (mEq/l), at the time of admission in tuberculous meningitis cases, were 4.9 ± 0.24 and 2.5 ± 0.13 respectively. Thus, the serum calcium levels were not high in tuberculous meningitis cases when compared to controls. But CSF calcium was significantly higher ($P < 0.01$) in tuberculous meningitis cases when compared to controls. Also we could not find any significant change in serum calcium level at any of the

subsequent follow-up, while CSF calcium was significantly higher at first follow-up (2.5 ± 0.09 mEq/l) in comparison to controls ($P < 0.001$). At second follow-up, mean CSF calcium decreased (2.4 ± 0.04 mEq/l) and it was insignificantly higher than that seen in the controls ($P > 0.05$) (Fig. 1 & 2). Our findings were found to be consistent with those obtained by other workers viz. McCance and Watchron (1931), Misra et al (1973) and Ahmad et al (1977). However, Kumar et al (1981) found an increase in both serum and CSF calcium in tuberculous meningitis.

Kumar et al (1981), observed that in controls plasma and CSF calcium levels (mEq/l) were 4.69 ± 0.69 and 3.00 ± 0.33 respectively, the corresponding values observed in cases of tuberculous meningitis were 5.57 ± 0.82 and 3.93 ± 0.54 respectively ($P < 0.001$ and $P < 0.001$ for plasma and CSF respectively). Authors further observed that plasma and CSF calcium values decreased with treatment, but still plasma calcium levels remained higher after three weeks of treatment ($P < 0.001$) as compared to controls. Authors suggested that the CSF calcium was elevated and corresponded with increased proteins in the CSF.

Serum and CSF magnesium in tuberculous meningitis :

It is evident from table 10 that the mean serum and CSF magnesium levels (1.7 ± 0.23 mEq/l and 1.9 ± 0.21

mEq/l respectively) were decreased in cases of tuberculous meningitis in comparison to controls ($P < 0.001$ and $P < 0.001$ for serum and CSF respectively) (Fig. 3 & 5). At first and second follow-up, mean serum magnesium levels (mEq/l) were 1.9 ± 0.22 and 1.9 ± 0.40 respectively, while the corresponding values for CSF magnesium (mEq/l) were 2.1 ± 0.20 and 2.1 ± 0.40. Thus, we observed that while both serum and CSF magnesium decreased in tuberculous meningitis, CSF magnesium values had a tendency to approach the values observed in plasma. Further, we found a rise in serum and CSF magnesium levels following the treatment, though the levels still remained significantly lower ($P < 0.05$) than those in control subjects (Fig. 4 & 6). Our findings were consistent with those of other workers viz. Cohen (1927), McCance and Watchron (1931), Chojnacki (1956), Rajvanshi et al (1970), Misra et al (1973), Ahmad et al (1977) and Praharaj et al (1982). Kumar et al (1981), also observed low levels of magnesium in serum and CSF but unlike the observations in our study and those of other workers, mentioned before, they found CSF magnesium levels were lower than that of serum.

Cohen (1927), attributed these changes in CSF magnesium, to increase in the permeability of choroid plexus and cerebrospinal vessels which get damaged by invading organisms or toxins. Thus there was a

decreasing concentration in CSF of those substances which were normally present in greater quantity in CSF than in the plasma. This was also suggested by Misra et al (1973) and Praharaj et al (1982). Ahmad et al (1977) concluded that the low CSF magnesium content in tuberculous meningitis was related to hypomagnesemic states, while Kumar et al (1981) attributed it to the blocking of extra magnesium entering from the brain tissue into the CSF pool.

As it is evident from table 19, out of 15 cases of tuberculous meningitis, 4 improved, 5 expired and 1 improved with sequelae, while 3 left the hospital against medical advice and 2 absconded. We found no significant difference ($P > 0.05$) in the mean CSF magnesium levels at the time of admission, between the group of 4 cases who improved and the group of 5 cases who expired (2.1 ± 0.15 mEq/l and 2.0 ± 0.11 mEq/l). Out of 5 cases who left against medical advice or absconded, 3 left after two follow-up investigations and were not improving. These 3 cases had the mean CSF magnesium level 1.7 ± 0.20 mEq/l at the time of admission, which was significantly lower ($P < 0.01$) than the levels found at admission in those cases which improved. Duration and severity of illness was almost similar in all these groups.

Serum and CSF calcium in acute bacterial meningitis :

As is shown in table 11, at the time of admission, mean serum and CSF calcium values (mEq/l) in cases suffering from pyogenic meningitis were 4.9 ± 0.16 and 2.4 ± 0.07 respectively. Thus, as in the cases of tuberculous meningitis, pyogenic meningitis cases also did not show any rise in serum calcium levels at the time of admission. However, a statistically insignificant rise ($P > 0.05$) in CSF calcium at the time of admission was observed as compared to controls (Fig. 1 & 2). Also, we did not observe any significant change in serum and CSF calcium at subsequent follow-ups in these cases. Similar findings were reported by Misra et al (1973).

Serum and CSF magnesium in acute bacterial meningitis :

It is evident from table 11, that mean serum and CSF magnesium levels (mEq/l), at the time of admission were 1.8 ± 0.13 and 1.9 ± 0.09 respectively and these were found to be significantly lower than those observed in controls ($P < 0.01$ and < 0.001) (Fig. 3 & 5). At first and second follow-up, mean serum magnesium levels (mEq/l) were 2.0 ± 0.24 and 2.1 ± 0.32 respectively, while the corresponding values for CSF magnesium (mEq/l) were 2.2 ± 0.40 and 2.2 ± 0.40 respectively (Fig. 4 & 6). Thus, a decrease was

observed in serum and CSF magnesium in pyogenic meningitis cases in comparison to the normal controls in a manner similar to those of tuberculous meningitis cases. Also the levels rose with treatment, though CSF magnesium still remained significantly lower ($P < 0.05$) than in the control subjects. Similar findings were reported by Misra et al (1973) and Praharaj et al (1982), who regarded these changes as a consequence of increased permeability of the cells of choroid plexus and cerebrospinal blood vessels following damage and invasion by organisms or toxins.

As is evident from table 19, out of 7 pyogenic meningitis cases 3 improved, 3 expired and 1 left against medical advice. Cases who improved had mean CSF magnesium level of 1.9 ± 0.07 mEq/l at the time of admission, while in those who expired corresponding mean CSF magnesium level was 2.0 ± 0.07. The difference between the two mean levels was statistically insignificant ($P > 0.05$). One case, who did not improve and left against medical advice after two follow-up investigations, showed that CSF magnesium was 1.82 mEq/l at the time of admission, the level decreased to 1.56 mEq/l at first follow-up and again rose to 1.79 mEq/l at second follow-up. The duration and severity of illness was almost similar in all the 3 groups of patients viz. those who improved, expired and left against medical advice.

Thus, we found that initial CSF magnesium levels could not probably predict the prognosis of a case in pyogenic meningitis. However, at subsequent follow-up if CSF magnesium did not increase, poor prognosis might be predicted as far as the recovery was concerned.

Serum and CSF calcium in Encephalitis :

As seen from table 12, mean serum and CSF calcium levels (mEq/l) at the time of admission were 4.9 $\pm$ 0.20 and 2.4 $\pm$ 0.09 respectively (Fig. 1 & 2). Statistically insignificant differences ($P > 0.05$) were observed in serum and CSF levels of calcium at the time of admission, when compared to corresponding calcium levels in control subjects. Also, no changes in serum and CSF calcium levels were observed at follow-up. Since no other author has done the study of serum and CSF calcium levels in encephalitis, comparison to other studies could not be done.

Serum and CSF magnesium in Encephalitis :

As shown in table 12, there were lower levels of mean serum and CSF magnesium levels (1.9 $\pm$ 0.20 mEq/l and 2.1 $\pm$ 0.09 mEq/l) in encephalitis, at the time of admission in comparison to controls (Fig. 3 & 5). At follow-up, serum and CSF magnesium showed higher levels, being 2.2 $\pm$ 0.07 mEq/l and 2.4 $\pm$ 0.12 mEq/l respectively

(Fig. 4 & 6). Thus, at the time of admission, we observed a significantly low serum and CSF magnesium levels in encephalitis ($P < 0.01$ and < 0.001) when compared to controls. Also a significantly higher mean CSF magnesium levels were found at first follow-up when compared to mean values at the time of admission ($P < 0.05$) in the same group of patients. No other worker has studied the CSF magnesium levels in encephalitis. Only Rajvanshi et al (1970) studied serum magnesium levels in encephalitis at the time of admission and found decreased levels in these cases as compared to controls.

Table 19 depicts the outcome of encephalitis cases. Out of 9 cases of encephalitis 6 improved, 2 expired and 1 left against medical advice. On comparing the mean CSF magnesium values at the time of admission, between the cases of encephalitis who improved and those who expired, an insignificant difference was found (2.1 ± 0.09 mEq/l and 2.1 ± 0.01 mEq/l respectively, $P > 0.05$). One case who left against medical advice, had CSF magnesium 2.07 mEq/l at the time of admission. Thus, probably, there was no relationship between the CSF magnesium levels, found at the time of admission, and prognosis in cases of encephalitis.

Serum and CSF calcium in epilepsy :

It is evident from table 13, that the mean serum and CSF calcium in epilepsy was 4.9 ± 0.26 mEq/l and 2.5 ± 0.18 mEq/l respectively at the time of admission. A comparison of these mean values to those of controls revealed no difference between the mean serum calcium levels (Fig. 1 & 2). Although, mean CSF calcium level was higher in cases of epilepsy, the difference with the controls was statistically insignificant ($P > 0.05$). Our findings were consistent with the observation of Kumar et al (1979).

Serum and CSF magnesium in epilepsy :

It is evident from table 13 that the levels of serum and CSF magnesium in cases of epilepsy were lower in comparison to levels found in controls. Mean serum and CSF magnesium levels (mEq/l) in epilepsy were found to be 2.1 ± 0.17 and 2.2 ± 0.14 respectively. The difference in comparison to controls was statistically insignificant ($P > 0.05$) in serum, while it was significant in CSF ($P < 0.05$) (Fig. 3 & 5). Our findings were consistent with those of other workers viz. Hanna et al (1960), Chhaparwal and Pohowalla (1966), Jain et al (1968) and Kumar et al (1979). Kumar et al (1979) observed significantly lower levels of both serum

and CSF magnesium in epilepsy cases as compared to controls. These authors did not give any reason for such decreased magnesium levels, but concluded that the lowered CSF magnesium in idiopathic epilepsy could be the possible etiopathogenetic mechanism in the production of convulsions in children.

SUMMARY AND CONCLUSION

SUMMARY AND CONCLUSION

Present work was carried out to study serum and cerebrospinal fluid (CSF) calcium and magnesium in children, suffering from acute neurological disorders. The work was conducted from May 1982 until March 1983, in the department of Paediatrics, M.L.B. Medical College, Jhansi (U.P.). This study comprised of forty children (from birth to 12 years of age) suffering from various acute neurological disorders. Eight age matched children not manifesting any neurological disorder served as control.

The primary aim of our study was to evaluate the serum and CSF calcium and magnesium in children suffering from tuberculous meningitis, acute bacterial meningitis, encephalitis and epilepsy. These electrolyte values obtained in patients were compared to those obtained in control. Besides evaluating the serum and CSF calcium and magnesium, various clinical features were also noted. Routine investigations viz. CSF cytology and biochemical examination were done in each case. It was also our endeavour to ascertain the possible inter-relationship between the clinical progress,

following treatment, and the subsequent changes in serum and CSF calcium and magnesium levels. With this objective in view, serum and CSF calcium and magnesium levels and other investigations were done at the time of initial contact and at one or two subsequent follow-up dates (5 to 10 days interval each).

Out of 40 cases suffering from neurological disorders, 15 had tuberculous meningitis, 7 had acute bacterial meningitis and 9 cases each were suffering from encephalitis and grand mal epilepsy.

Statistical analysis was done to derive mean and standard deviation. Comparison of mean values, wherever indicated, was done using student 't' test.

Serum and cerebrospinal fluid calcium :-

In the control group, mean serum calcium level was found to be almost double (4.9 $\pm$ 0.22 mEq/l) than that observed in CSF (2.3 $\pm$ 0.12 mEq/l).

Mean serum calcium levels (mEq/l) at initial contact, in tuberculous meningitis, acute bacterial meningitis, encephalitis and epilepsy cases were found to be 4.9 $\pm$ 0.24, 4.9 $\pm$ 0.16, 4.9 $\pm$ 0.20 and 4.9 $\pm$ 0.26 respectively. It is evident from these findings that the mean serum calcium levels in our study groups were

not significantly different from the control subjects. Moreover, at subsequent follow-up, no significant change was observed in the mean serum calcium levels of these patients.

Mean CSF calcium levels (mEq/l) at the time of initial contact in tuberculous meningitis, acute bacterial meningitis, encephalitis and epilepsy were found to be 2.5 ± 0.13, 2.4 ± 0.07, 2.4 ± 0.9 and 2.5 ± 0.18 respectively. Out of all these values, only the mean value in tuberculous meningitis was significantly higher as compared to control. Like the serum calcium levels, the CSF calcium too, did not undergo a significant change at subsequent follow-up dates.

Serum and cerebrospinal fluid magnesium :-

In contrast to the levels of calcium, magnesium levels were found to be higher in CSF (2.6 ± 0.16 mEq/l) than in serum (2.2 ± 0.22 mEq/l), in the control group.

Mean serum magnesium levels (mEq/l) at initial contact, in tuberculous meningitis, acute bacterial meningitis, encephalitis and epilepsy were found to be 1.7 ± 0.23, 1.8 ± 0.13, 1.9 ± 0.20 and 2.1 ± 0.17 respectively. It is evident from these findings, that barring the mean serum magnesium levels in epilepsy, which revealed insignificant difference from the control,

values in the other 3 groups of cases (tuberculous meningitis, acute bacterial meningitis and encephalitis) were significantly lower as compared to the control values. However, at subsequent follow-up, a gradual rise in the mean serum magnesium levels was observed in all study groups.

Mean CSF magnesium levels (mEq/l) at initial contact in tuberculous meningitis, acute bacterial meningitis, encephalitis and epilepsy were found to be 1.9 ± 0.21, 1.9 ± 0.09, 2.1 ± 0.09 and 2.2 ± 0.14 respectively. It is evident that all these values were found to be significantly lower in comparison to control. Similarly, although at subsequent follow-up periods, a gradual rise was observed in mean CSF magnesium levels in all these groups of patients, yet the levels remained lower in comparison to control cases.

From this study, it was found that initial CSF magnesium levels could not probably predict the prognosis of a case of tuberculous meningitis, acute bacterial meningitis or encephalitis. However, at subsequent follow-up, if CSF magnesium did not increase, poor prognosis might be predicted in tuberculous meningitis and acute bacterial meningitis cases as far as the recovery was concerned.

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APPENDIX

CASE-SHEET

Name : Diagnosis :

Age : Sex : Male/Female

Father's Name:

Address :

Occupation : Father Mother:

Total income of family :

Per capita income :

Birth order of child :

Geniological tree :

Dietary History :

	Started at age	Upto age
Breast milk		
Artificial milk only		
Added artificial milk		
Solids added		

Present diet :

Immunization History :

	Small pox	B.C.G.	Polio(oral)	DPT(Triple)
I				
II				
III				
IV				
V				

Antenatal, natal & postnatal history :

Uneventful/Any significant history

Mile Stones :

	Age
Social smile	
Neck Holding	
Sitting	
Crawling	
Standing	
Walking	
Speaking-	
Monosyllables	
Handling of spoon	

Family History :

Present illness:

Past Illness :

Definite H/o Primary complex
H/o Pertussis
Measles
Ear Discharge
Head Injury
Convulsions

Clinical Examination :

General appearance : Healthy/Malnourished

Head circumference :

Chest circumference :

Weight :

Anterior fontanelle :

Lymphadenopathy : Significant / Insignificant

Other significant positive finding :

C.N.S.	Date		
Level of consciousness (Conscious, Stage I - Stupor			
Stage II - Light coma,			
Stage III - Deep coma,			
Stage IV - Patient flacid & apneic)			
Posture (Normal, Decorticate Decebrate)			
Speech			
Gait			
Signs of Meningeal Irritation			
Neck Rigidity			
Kernigs signs			
Brudzinski's sign			
Fundus examination			

Cranial Nerves (Affected, Not affected)	Date		
II (Optic Nerve)			
III (Occulomotor Nerve)			
IV (Trochlear Nerve)			
VI (Abducent Nerve)			
VII (Facial Nerve)			
Others			

Motor System

Lower limbs

	Right lower limb			Left lower limb		
	Date			Date		

(I) Power

Hip

Extensors

Flexors

Adductors

abductors

Rotators

Knee

Flexors

Extensors

Ankle

Planter flexors

Dorsi flexors

Invertors

Evertors

(II) Bulk

(III) Tone

(IV) Co-ordination

(V) Involuntary movements

Motor System

Upper limbs

	Right upper limb			Left upper limb		
	Date			Date		

(I) Power

Shoulder

Motor System

Upper limbs

	Right upper limb			Left upper limb		
	Date			Date		
Adductors						
Abductors						
Rotators						
Elbow						
Flexors						
Extensors						
Supinators						
Pronators						
Wrist						
Flexors						
Extensors						
Abductors						
Adductors						
Fingers						
Flexors						
Extensors						
Abductors						
Adductors						
Opponeus action						
(II) Bulk						
(III) Tone						
(IV) Co-ordination						
(V) Involuntary movements						

Sensory System

	Upper limbs		Lower limbs	
	Right	Left	Right	Left
(I) Touch				
Fine				
Coarse				
(II) Pain				
(III) Temperature				
(IV) Position & joint sense				
(V) Vibration				
(VI) Cortical sensations				
Two point discrimination.				
Stereognosis				
Topognosis				
Borognosis				

Any significant change in follow up :

Date

Reflexes : Superficial

1) Corneal Right
Left

2) Conjunctival Right
Left

3) Pupillary (Direct & consensual) Right
Left

4) Abdominal Right
Left

5) Cremastric Right
Left

6) Planters Right
Left

Date

Reflexes : Deep

1) Biceps Right
Left

2) Triceps Right
Left

3) Supinator Right
Left

4) Knee Right
Left

5) Ankle Right
Left

6) Ankle clonus Right
Left

7) Patellar clonus Right
Left

8) Jaw Jerk

Cerebellar signs Date

Extrapyramidal signs Date

C.V.S. Date

Normal
Any abnormality

Resp. System

Normal
Any abnormality

Abdomen

Liver
Spleen
Any other

INVESTIGATIONS

	Date		

Blood

- Haemoglobin
- T.L.C.(/cubic mm.)
- D.L.C. (%)
 - P
 - L
 - E
 - M
- E.S.R.(Wintrobe) (mm for Ist hour)
- S. Calcium
- S. Magnesium

C.S.F.

- Tension
- Colour
- Coagulum
- Protein
- Sugar
- Chloride
- Cells
- Gram's Staining
- Culture & Sensitivity
- C.S.F. Calcium
- C.S.F. Magnesium

X-ray chest P.A. View :
(If necessary)

X-ray skull A.P.) View :
(If necessary) Lat.)

Montoux test :
(If necessary)

Others :
